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INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification 6 :
A61K 51/00, A61B 6/00, A61F 5/00

A1

(11) International Publication Number: WO 96/34632

(43) International Publication Date: 7 November 1996 (07.11.96)

(21) International Application Number: PCT/US96/06240

(22) International Filing Date: 3 May 1996 (03.05.96)

(30) Priority Data:

08/433,674	4 May 1995 (04.05.95)	US
08/538,095	2 October 1995 (02.10.95)	US
08/584,646	11 January 1996 (11.01.96)	US

(71) Applicant (*for all designated States except US*): THE REGENTS OF THE UNIVERSITY OF MICHIGAN [US/US]; 3003 South State Street, Ann Arbor, MI 48109 (US).

(72) Inventors; and
(75) Inventors/Applicants (*for US only*): WAHL, Richard, L. [US/US]; 3572 Delhi Overlook, Ann Arbor, MI 48103 (US). ZASADNY, Kenneth, R. [US/US]; 1592 Superior Boulevard, Wyandotte, MI 48192 (US).

(74) Agents: MOGA, Thomas, T. et al.; Harness, Dickey & Pierce, P.L.C., P.O. Box 828, Bloomfield Hills, MI 48303 (US).

(81) Designated States: AU, CA, JP, US, European patent (AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE).

Published
With international search report.
Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.

(54) Title: METHOD OF ESTABLISHING THE OPTIMAL RADIATION DOSE FOR RADIOPHARMACEUTICAL TREATMENT OF DISEASE

(57) Abstract

A method for determining the number of millicuries to be administered to a patient so as to deliver a given centigray (cGy) dose to either the patient's lean body of the patient's total body. The method includes the steps of injecting a radioactive tracer into a patient, determining radiation levels in the whole body, calculating a geometric mean based on the radiation levels, determining the percent-injected activity remaining in the body at each time point, plotting the percent-injected activity versus calculated time from infusion on a log-linear graph, determining the effective half-life and the rate of clearance from the log-linear graph, cross-indexing the effective half-life value with the patient's body weight, and multiplying the determined amount of therapeutic millicuries per centigray by the amount of desired centigray to be administered.

U.S. Patent Application
Serial No. 09/326,502
Filed – June 04, 1999
Atty Dkt –COUL-005/04US
Cooley Godward LLP (650) 843-5000
F1

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At present, the radiopharmaceutical is commonly introduced into the blood for ultimate internal distribution through conventionally known methods such as through intravenous, inhalation, or oral administration. A common unit of radioactivity is the millicurie, or mCi.

The general difficulty of the administration of radiopharmaceuticals for therapy lies in the fact that if the patient is given too much radioactivity, toxicity results. On the other hand, it is necessary to give enough of the radiopharmaceutical so that the disease is successfully treated. The most common specific side effect of radiopharmaceutical treatment is bone marrow suppression or ablation. This is caused by the targeting of the radiopharmaceutical (or the radiolabel) to the bone or bone marrow or is due to circulation of the radioantibody through the blood vessels (including the marrow). In general, this situation could lead to bleeding, infection or death. This side effect (as well as other undesirable side effects) is caused by the inaccuracy of known methods used to determine the radioactive dose for the individual patient. For example, up to a five fold difference in the radiation dose to blood, bone marrow, or body received/mCi of the particular radioantibody administered may exist between patients. (Radiation dose is defined as the total amount of energy per unit mass deposited in an individual as a result of radioactive decay.) These differences are tied to the fact that individuals are physiologically different. Not only are individuals of different sizes and, to some degree, densities, they also differ in abilities to metabolize and clear radiopharmaceuticals. For example, if the radioactivity is attached to a monoclonal antibody, the radioactivity might be eliminated from different patients such that a half life of clearance of radioactivity of three days might be identified in a first patient, while a half life of clearance of radioactivity of six days is identified in a second patient.

Accordingly, the challenge facing the physician today is determining the correct number of millicuries to be administered to a particular patient having a particular disease at a particular stage of development of that disease. The number of millicuries to be administered is based on the prescription of a

METHOD OF ESTABLISHING THE OPTIMAL RADIATION DOSE FOR RADIOPHARMACEUTICAL TREATMENT OF DISEASE

BACKGROUND OF THE INVENTION

1. Field of the Invention

The present invention relates to the administration of radiopharmaceutical compounds for the therapy of disease including cancer. More particularly, the present invention relates to a method of establishing the optimal effective radiation dose for treatment of disease, the method minimizing toxicity while preserving therapeutic activity.

2. Description of the Relevant Art

Radiopharmaceuticals are compounds composed of radioactive isotopes often bound to other molecules. These radiopharmaceuticals are used in assessing the presence, outline, size, position, or physiology of individual organs or tissues. More significantly for the present invention, radiopharmaceuticals are commonly used in the treatment of disease. For example, radioactive iodine (I-131) is used to treat thyroid cancer or overactive thyroids (Grave's disease). Of considerable importance is the development of monoclonal antibodies having attached radioactive labels. When combined with antibodies that are relatively specific for a particular diseased tissue, such antigen-specific monoclonal antibodies are able to selectively direct comparatively sizable amounts of radiation to the specific disease site. Such treatments are being applied to the treatment of non-Hodgkin's lymphomas, Hodgkin's lymphomas, Hepatoma, colo-rectal cancer, brain tumors, and many other forms of cancer. In addition, the treatments also have the potential to treat other types of disease, including auto-immune conditions such as, for example, Systemic Lupus and Rheumatoid arthritis. Targeted radiopharmaceutical therapy may be ultimately be found to be broadly applicable to a wide variety of neoplastic and benign diseases.

given radiation dose to the "whole body" of the patient, which is dependent upon several factors, including the patient's size and the rate of disappearance of radioantibody from the body as determined by direct measurements of the biodistribution of a tracer dose (a small, non-therapeutic quantity) of radioactivity using a gamma camera, probe detector system, or other radiation detection system. Using such an approach, a "whole body radiation dose" can be calculated from the tracer doses, which can be used to predict the radiation dose the "whole body" would receive from subsequent radiopharmaceutical therapy and which allows the radiation dose administered to be effective. Initial results with this approach using the anti-B-1 antibody have shown excellent therapeutic efficacy and modest toxicity. Results of clinical studies with this approach are detailed in NEJM 7:329, pp. 459-465, 1993 (Kaminski et al.), J. Nucl. Med. 35(5), 233P, 1994 (Wahl et al.), and J. Nucl. Med. 35(5), 101P, 1994 (Wahl et al.).

While this approach to calculating "whole body" radiation dose represents a major improvement over other methods which are not individualized to the patient's individual pharmacology, it still does not fully overcome the difficulties related to the accurate calculation of optimal radiation doses to treat radiosensitive tumors. The inherent failure of this method lies in the fact that the simple assumptions of "whole body" dose are not fully valid in terms of human patient physiology. Accordingly, while radiotoxicity is reduced, it is not fully eliminated or even absolutely minimized. Part of the reason for this failure is that the "whole body" dose approach assumes that a radiopharmaceutical is uniformly distributed throughout the body. There is an assumption underlying this thinking that the body is uniform, and that distribution of chemicals in the body is likewise uniform. This is not the case, as most radiopharmaceuticals, particularly intact monoclonal antibodies, have very limited accumulation in fat tissue compared to considerably greater accumulation in lean body tissue (including bone marrow).

In an effort to improve the accuracy of radiopharmaceutical mCi dosage, a method has been developed that utilizes a parameter directed to

"total body dose-lean" (TBD-lean) to account for the fact that individuals may be modeled as an outer shell of fat (where little radioantibody or radiopharmaceutical accumulation occurs) which surrounds an active lean body mass, including bone marrow.

By appreciating the fact that in man there is a "lean body" within a "fat" outer shell, a formula may be used to estimate what percentage of the person is fat and what percent of the person is lean. Thereafter, the radioactivity is traced as essentially being distributed uniformly and totally through the lean component. By first estimating what fraction of the body is lean and then calculating the radioactivity distribution within a given lean volume, the proper dose of radiopharmaceutical for treatment without undue toxicity can be administered on an individualized, case-by-case basis.

While resolving many of the difficulties related to the prescription of effective amounts of radiation doses, the prior art nevertheless may be improved upon.

SUMMARY OF THE PRESENT INVENTION

The present invention is directed to methods for determining the number of millicuries of radioactivity to be administered to a patient so as to establish a given centigray (cGy) dose to either the patient's lean body or the patient's total body.

According to a general method of the present invention, a parameter directed to "total body dose-lean" (TBD-lean) is utilized to account for the fact that individuals may be modeled as an outer shell of fat (where little radioantibody or radiopharmaceutical accumulation occurs) which surrounds an active lean body mass, including bone marrow. By appreciating the fact that in man there is a "lean body" within a "fat" outer shell, a formula may be used to estimate what percentage of the person is fat and what percent of the person is lean. Thereafter, the radioactivity is traced as essentially being distributed uniformly and totally through the lean component. By first estimating what fraction of the body is lean and then calculating the

radioactivity distribution within a given lean volume, the proper dose of radiopharmaceutical for treatment without undue toxicity can be administered on an individual, case-by-case basis.

According to a modified method of the present invention, the following steps are followed.

Initially the rate of clearance or disappearance of radioactivity from a patient is determined by direct measurement across multiple time points using a radiation detection device (such as a NaI probe or a gamma camera). This step determines changes in the radiation concentration of a particular patient over a given period of time. For example, a series of measurements, commonly seven or eight, are done over a period of a week with the first measurement made immediately following a tracer injection of the radiopharmaceutical. The time in hours is determined from the end of the tracer infusion for each measurement, resulting in a variety of values. Appropriate measurement is made of the amount of radioactive disintegration measured from the front of the patient (anterior measurements) and/or from the back of the patient (posterior measurements).

Based on these readings, a geometric mean is calculated. The geometric means may be based upon daily NaI probe measurements, but may also be based upon anterior and posterior conjugate view gamma camera imaging data or other methods of radiation detection. According to the conjugate view approach, a geometric mean is calculated for each time point by multiplying the anterior and posterior readings and determining the square root of the total figure. This mean represents an average number of counts. The background counts are subtracted for a corrected mean. The percent injected activity remaining in the body for each time point is thereafter determined by dividing the counts at a given time by the counts immediately after the tracer is injected. Thereafter, the percent of injected activity versus the calculated time from infusion is plotted on a log linear graph. With these points established on the log linear graph, a line is drawn to determine the

cumulated Activity Hours

residence time

intersection of the best fit line with the 50% injected activity line, thereby determining effective half life, or T 1/2-effective.

With T 1/2-effective thus established and the patient's body weight known, these values are cross-indexed on either a graph (the "graphical" approach) or on a table (the "tabular" approach) to determine the recommended millicuries per centigray (mCi per cGy) to be administered (activity per unit TBD or TBD-lean). (Both the graphical approach and the numerical approach represents activity per unit for total body dose [TBD] or total body dose-lean [TBD-Lean] as a function of total body or lean body mass and T 1/2-effective.) Both the graphical and numerical approaches (and their expressed quantities) are features of the present invention.

MTD

The actual amount of therapeutic millicuries is then determined by multiplying the recommended mCi per cGy by the amount of desired centigray to be administered.

While the present invention is described as having application to total body dose and total body dose-lean, the method of the present invention is also applicable to dosimetry to blood, bone marrow, and other organs and tissues such as the lung, the liver, and the kidney.

These and other features of the present invention are best understood from the following specification, drawings and examples.

BRIEF DESCRIPTION OF THE DRAWINGS

Figure 1 is a graph illustrating the relationship of the fat component of the individual with respect to the lean component of the same individual, thus defining the "lean person within the fat person" theory of the present invention; and

Figure 2 is a graph illustrating the elimination of the radioactive element from the individual over time, with the amount of material being on the Y-axis and time being on the X-axis.

Figure 3 is a blank worksheet onto which are to be entered all necessary intermediate values based upon observations of clearance of the

tracer from the body according to an alternate method of the present invention;

Figure 4 is a curve set on a graph indicating therapeutic activity per unit dose calculated from data acquired on days 0, 3, and 7 versus data acquired on days 0, 1, 2, 3, 4, 5, 6, and 7;

Figure 5 is a blank graph consisting of a log linear graph onto which pertinent elimination values are to be marked at different intervals of time;

Figure 6 is similar to the graph of Figure 4 but illustrating two series of elimination values for two sample patients;

Figure 7 is a fused image of a cross-sectional view of the central body compartment of a sample patient following administration of radiolabelled antibodies;

Figure 8 is a graph illustrating the relationship of the fat component of the individual with respect to the lean component of the same individual;

Figures 9a - 9p define a series of graphs used for determining the therapeutic mCi/cGy to be administered based on known T 1/2-effective and the patient's mass (in Kg), total body mass (in Kg) for TBD, and lean body mass (in Kg) for TBD-Lean;

Figures 10a - 10h define a series of tables used for determining the therapeutic mCi/cGy to be administered based on known T 1/2-effective and the patient's mass (in Kg), total body mass (in Kg) for TBD, and lean body mass (in Kg) for TBD-Lean;

Figure 11 is a three-dimensional graph based on the series of graphs of Figures 9a - 9p;

Figure 12 is chart summarizing the input and output data of twenty-one sample patients;

Figure 13 is a toxicity versus mCi/Kg graph with the data points of the twenty-one sample patients of Figure 12;

Figure 14 is a toxicity versus total body dose [cGy] graph with the data points of the twenty-one sample patients of Figure 12; and

Figure 15 is a toxicity versus total body dose-lean [cGy] graph of the data points of the twenty-one sample patients of Figure 12.

DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENT

According to the theory underlying the general method of the present invention, the body represents two major compartments, a "fat" compartment and a "lean" compartment and that the "lean" person resides within an outer shell of "fat". These related theories represent a major departure from other approaches to dosimetry. Accordingly, a calculation of the quantity of the patient which is "lean body mass" can be made. From this new mass and new shape, a new and more accurate radiation dose can be determined to the "lean body" using methods of least squares fitting of kinetic radioantibody or radiopharmaceutical clearance data and assumptions of non-uniform distribution of radioactivity between the two body compartments. From this is produced one simple assumption that all radioactivity resides in the "lean" compartment, while none resides in the fat compartment, which encases the "lean" compartment. With the further assumption that the bone marrow is part of the freely accessible "lean" compartment, a beta particle and photon dose to the lean compartment can be determined. It is further assumed in this approach that irradiation of the "fat" layers has either no significant or has little significant adverse effects on bone marrow function.

I. GENERAL METHOD

Figure 1 illustrates the relationship of the fat component of the individual with respect to the lean component. An individual can be thought of as two ellipsoids, with the length x-1 or x-2 and with y-1 or y-2. The outer ellipsoid, labelled OE, with the larger x and y dimensions represents fat plus lean mass, with a volume (in liters) approximately equal to the patient's weight (in kilograms). The inner ellipsoid, labelled IE, with the same aspect ratios, is defined in liters by the formulae:

$$45.5 + 0.91(\text{height-152}) = \text{Lean Body Mass (for women)}$$

$$48.0 + 1.06(\text{height-152}) = \text{Lean Body Mass (for men)}$$

(where height is in centimeters)

It should be understood that total Lean Body Mass could also be directly measured by CT, x-ray absorptiometry, immersion weighing, and other known methods. The total body absorbed dose is then determined for the lean body ellipsoid based on conventional calculations. It should also be understood that corrections for Compton scatter of photons from the fat compartment or some trace accumulation in the fat compartment are also possible, but need not be included in the simplest application of the present method.

The steps of the method for applying the present invention are as follows, and reference may be had throughout the following explanation to Example 1 which appears below.

A "Proposed Lean Body Radiation Dose" is determined. This is a variable and can be selected from a wide range of possibilities. The proposed lean body dose shown in the "Data Entry" of Example 1 is 75 and is based on the particular antibody used. The value 75, however, should be interpreted as being a representative range. (It is to be understood that while Example 1 is directed to the use of an antibody, the methods of the present invention may be more generally used with any protein or compound having specificity for a target cell or a target substance, provided the protein or compound is capable of carrying a radioactive marker or label. For example, newly developed phospholipidethers having cancer-cell specificity may be radiolabelled and used in the method of the present invention.)

Thereafter, the "Patient Lean Body Mass" is determined from the formula set forth above or other methods. In Example 1, the subject was a male, and the value (in kilograms) was found to be 65.00.

The "Tracer Dose" (in mCi) represents a the amount of radioactivity (the "Tracer Dose") that is initially administered to the patient. The course and timing of the elimination of the "Tracer Dose" is thereafter followed. The course of elimination is illustrated in Example 1 under the "Whole Body Probe Data".

As shown, the "Tracer Dose" was injected over a period of 40 minutes ("Start of Infusion: 3:50 PM; End of Infusion: 4:20 PM"). A whole body radioactivity probe is used to thereafter determine the amount of radioactive material still remaining in the body after certain intervals of time. (The whole body probe is only one of several possible ways of measuring the radioactivity in the patient. Other possible methods include a gamma camera, a geiger counter, whole-body counter, etc.)

In Example 1, the test intervals are separated by approximately 24 hours, as may be seen by reference to "Data Points" 1 through 8. Specifically, counts are done using the same radiation detection device from both anterior and posterior views. This is the so-called "conjugate view approach" and allows both front and back views of the patient and determination of a geometric mean of counts. ("P Intv" refers to length of the counting in seconds; the "Bkg counts" refers to background counts.)

Thereafter, and with reference to the "Data Analysis" of Example 1, a plot illustrating the disappearance of the radiation from the patient as determined by the probe is graphed. The plot of Example 1 is represented in Figure 2 showing time intervals (in hours) along the X-axis and the amount remaining along the Y-axis. On the "Data Analysis", a calculation has been done demonstrating the percentage of radioactive material (in this instance, radioactive iodine) that remains in the patient at a given time. With 100% of the dose being present at the beginning of the study, this amount is seen as disappearing over a period of time.

By referring to a trapezoidal integration determination (on the "Dosimetry Analysis" of Example 1), the area under the curve of the elimination graph (shown as an example in Figure 2) can be determined. (This can also be done using the "Curve Fitting" approach also illustrated under "Dosimetry Analysis" which utilizes a series of curve-fitting coefficients.) This represents accumulated radiation exposure to the patient. With this amount known, the "Long Term Behavior Extrapolation" ("Data Analysis") is used to provide information as to how quickly the radioactive material is leaving the body.

(There are listed three "Options" listed: "last 2pts., last 3 pts., last 4 pts." This is from the tail end of the disappearance of a curve such as that shown in Figure 2. At "last 3 pts.", the extrapolated T 1/2 is 67.85 hours.)

Knowing the area under the curve and knowing, according to the provided example, that the lean body mass is 65 kilograms, a "Determination of Photo Absorbed Dose From Lookup Table" is then made. ("Lookup Table" follows "Dosimetry Analysis".) This determines what component of the dose is due to an absorbed photon in addition to the dose due to beta decay (electrons). The "Lookup Table" is photon energy specific. An example of I-131 is shown.

Now, knowing the size of the mass (in this instance, 65 kilograms) and the dimensions of the ellipsoid, the amount of radiation dose to lean body mass can be calculated. In Example 1, 60% of the radiation dose to lean body mass is due to electrons and 40% is due to photons. Accordingly, to produce the exemplary 75 rads, it is necessary in this particular case to give the patient a dose of 76.6 mCi, as the radiation dose to lean body mass/mCi is 0.9785. It is coincidental that the mCi dose approximates the rad dose.

As may be seen, the object of the present invention and the described steps is to identify the estimated dose in mCi (presented under "Estimated Dose" under "Dosimetry Analysis"). Overall, the "Estimated Dose" is determined by sequential sampling (in Example 1 particular case there were eight time points) using a radioactivity detector. The necessary probe data is determined by using either a trapezoidal integration formula or a curve fitting formula. This is directed to the determination of the area under the curve which is accumulated radiation. Then, using the body size, the amount of photons absorbed versus the amount of photons not absorbed becomes known as well as the beta component.

The general method of the present invention may be more fully understood by reference to the following example.

EXAMPLE 1

Data Entry

Patient: John Doe		*Study:*	Dx-1(685+15mg)
Reg. num.:	12345678	*Analysis Date:*	22-Jun-95
Proposed Lean TB dose [cGy]:	75		Date / time
Patient height [cm]:	179	*Start of Infusion:*	14-Jun-95 3:50 PM
Patient weight [kg]:	90.00	*End of Infusion:*	14-Jun-95 4:20 PM
Patient sex [M/F]:	M		
Patient lean body Mass[kg]:	76.50	Interval of infusion:	0.50 hrs
Tracer Dose[mCi]:	5.100		
Therapy Dose[mCi]:	76.5		
Number of time points:	8		

Whole Body Counting Data: Whole body probe data

Data Point	Date / time	Patient: Ant. counts	Patient: Post. counts	P Intv[sec]	Bkg counts	Bkg Intv[sec]	Pat Net[cps]
Pre-inf bkg	24-Jan-90 12:00 PM	0	0	60.00	0	60.00	0.00
				60.00		60.00	0.00
				60.00		60.00	0.00
1	14-Jun-95 4:31 PM	47411	47391	60.00	80	60.00	788.68
2	15-Jun-95 8:12 AM	46881	38609	60.00	101	60.00	707.39
3	16-Jun-95 8:08 AM	38542	31381	60.00	101	60.00	577.94
4	17-Jun-95 8:15 AM	32076	25880	60.00	88	60.00	478.73
5	18-Jun-95 9:15 AM	23551	19913	60.00	83	60.00	359.55
6	19-Jun-95 9:50 AM	18945	16412	60.00	90	60.00	292.38
7	20-Jun-95 9:20 AM	16105	12582	60.00	91	60.00	235.73
8	21-Jun-95 9:10 AM	11838	9491	60.00	91	60.00	175.15
	last time point value must go here				cps at end of infusion =		788.68

Data Analysis

Patient: John Doe
Reg. num.: 12345678

Study: Dx-1(685+15mg)
Analysis Date: 22-Jun-96

Whole body probe data

Data Point	Time(hrs)	%I131	%ID	%ID/g	Trapezoidal cell Integrals:
Start of Infus.	0.00	0.00	0.00	0.000000	
End of infus.	0.50	99.82	100.00	0.001307	24.96
End of Infus.	0.50	0.00	0.00	0.000000	0.00
End of Infus.	0.50	0.00	0.00	0.000000	0.00
1	0.68	99.76	100.00	0.001307	9.14
2	16.37	89.53	94.94	0.001241	1484.33
3	40.30	73.15	84.51	0.001105	1946.74
4	64.42	60.59	76.32	0.000998	1612.68
5	89.42	45.51	62.69	0.000820	1326.23
6	114.00	37.01	55.68	0.000728	1014.22
7	137.50	29.84	48.83	0.000638	785.39
8	161.33	22.17	39.52	0.000517	619.71

Long Time Behavior Extrapolation: I-131 Tp 1/2 193.44 hrs

Time (hrs)	%I131	ln(%I131)
0.00	0.00	
0.50	99.82	4.603
0.50	0.00	
0.50	0.00	
0.68	99.76	4.603
16.37	89.53	4.495
40.30	73.15	4.292
64.42	60.59	4.104
89.42	45.51	3.818
114.00	37.01	3.611
137.50	29.84	3.396
161.33	22.17	3.099

slope	intercept	option	T 1/2 extrap	T 1/2 biol
-0.0125	5.1096	last 2 pts.	55.60	78.02
-0.0108	4.8588	last 3 pts.	63.99	95.61
-0.0099	4.7256	last 4 pts.	69.90	109.46

Yields an extrap. T1/2: 63.99 [hrs]

Last time point value: 22.17 [%I131]

Dosimetry Analysis

Patient: John Doe
Reg. num.: 12345678

Study: Dx-1(685+15mg)
Analysis Date: 22-Jun-96

Whole body probe data

Trapezoidal integration of %I-131:

Integral to last data point:	8823.40	[%I131-hr]
Int from last pt to inf(Textrap 1/2):	2046.81	[%I131-hr]
$\int_0^\infty dt$ %I-131(t) =	10870.21	[%I131-hr]

Curve fitting of %ID:	(biexponential)	
y = biexpfit(a,b,c,d)		
	Value	Error
a		
b		
c		
d		
Chisq		
R		

	Curve fitting (biexponential)	Trapezoidal integration		%difference
Residence Time:	0.00	108.70	[hrs]	#DIV/0!
Effective T1/2:	0.00	75.35	[hrs]	
Kinetics:				
AUC(0,∞):	#DIV/0!	[%ID-hr]		
AUMC(0,∞):	#DIV/0!	[%ID-hr^2]		
Mean system res time:	#DIV/0!	[hrs]		

Determination of photon absorbed dose from table lookup:

Pat'nt LBM:	76.50	[kg]
	77.00	[rounded to nearest kg]
$\Sigma\Delta\phi$(phot):	0.281010	[g-rad/µCi-hr]
$\Sigma\Delta\phi$(elec):	0.408500	[g-rad/µCi-hr]
$\Sigma\Delta\phi$(total):	0.689510	[g-rad/µCi-hr]

Dosimetry Results:

	Electron	frac of total	Photon	frac of total	Total	
Estimated Dose:	0.5805	59%	0.3993	41%	0.9798	[rad/mCi]
	0.01569		0.01079		0.02648	[cGy/MBq]
76.5 mCi therapy:	44.4		30.6		75.0	[rad]
2832.3443 MBq						[cGy]

TABLE (LOOKUP)

$\Sigma\Delta_e$ for photons from I-131 activity uniformly distributed in ellipsoids:

Mass (kg)	$\Sigma\Delta_e$ (photon) [g-rad/µCi-hr]	$\Sigma\Delta_e$ (elctrn)
2	0.0932	0.4085
4	0.1206	
6	0.1379	
8	0.1515	
10	0.1620	
20	0.1986	
30	0.2214	
40	0.2384	
50	0.2528	
60	0.2645	
70	0.2748	
80	0.2836	
90	0.2922	
100	0.2994	
120	0.3136	
140	0.3264	
160	0.3386	
180	0.3495	
200	0.3604	

Cubic spline interp lookup table:

Mass (kg)	$\Sigma\Delta_e$ (photon)
1	0.079500
2	0.093200
3	0.106900
4	0.120600
5	0.129250
6	0.137900
7	0.144700
8	0.151500
9	0.156750
10	0.162000
11	0.166480
12	0.170960
13	0.174990
14	0.179010
15	0.182620
16	0.186230
17	0.189480
18	0.192730
19	0.195660
20	0.198600
21	0.201270
22	0.203940
23	0.206390
24	0.208830
25	0.211080
26	0.213320
27	0.215410
28	0.217490
29	0.219450
30	0.221400
31	0.223250
32	0.225110
33	0.226870
34	0.228640
35	0.230330
36	0.232020
37	0.233640
38	0.235270
39	0.236830
40	0.238400
41	0.239920
42	0.241430
43	0.242900
44	0.244370
45	0.245790
46	0.247220
47	0.248590
48	0.249960
49	0.251280
50	0.252600
51	0.253870
52	0.255140
53	0.256370
54	0.257590
55	0.258780
56	0.259960
57	0.261110
58	0.262260
59	0.263380
60	0.264500
61	0.265580
62	0.266690
63	0.267750
64	0.268820
65	0.269850
66	0.270890
67	0.271880
68	0.272880
69	0.273840
70	0.274800
71	0.275720
72	0.276640
73	0.277520
74	0.278410

75	0.279260	114	0.309400	153	0.334450
76	0.280150	115	0.310110	154	0.335050
77	0.281010	116	0.310820	155	0.335650
78	0.281870	117	0.311520	156	0.336250
79	0.282730	118	0.312220	157	0.336850
80	0.283600	119	0.312910	158	0.337440
81	0.284480	120	0.313600	159	0.338020
82	0.285360	121	0.314280	160	0.338600
83	0.286240	122	0.314950	161	0.339170
84	0.287120	123	0.315620	162	0.339740
85	0.288000	124	0.316280	163	0.340300
86	0.288870	125	0.316930	164	0.340870
87	0.289720	126	0.317580	165	0.341420
88	0.290570	127	0.318230	166	0.341970
89	0.291390	128	0.318880	167	0.342520
90	0.292200	129	0.319510	168	0.343070
91	0.292970	130	0.320150	169	0.343610
92	0.293740	131	0.320780	170	0.344150
93	0.294470	132	0.321410	171	0.344690
94	0.295210	133	0.322040	172	0.345230
95	0.295910	134	0.322660	173	0.345760
96	0.296620	135	0.323280	174	0.346300
97	0.297320	136	0.323910	175	0.346830
98	0.298010	137	0.324530	176	0.347360
99	0.298710	138	0.325160	177	0.347900
100	0.299400	139	0.325780	178	0.348430
101	0.300100	140	0.326400	179	0.348970
102	0.300800	141	0.327020	180	0.349500
103	0.301510	142	0.327650	181	0.350040
104	0.302220	143	0.328270	182	0.350570
105	0.302940	144	0.328890	183	0.351110
106	0.303660	145	0.329520	184	0.351650
107	0.304380	146	0.330140	185	0.352200
108	0.305100	147	0.330760	186	0.352740
109	0.305820	148	0.331380	187	0.353280
110	0.306540	149	0.332000	188	0.353830
111	0.307260	150	0.332620	189	0.354370
112	0.307970	151	0.333230	190	0.354920
113	0.308690	152	0.333840	191	0.355460

192	0.356010
193	0.356560
194	0.357110
195	0.357650
196	0.358200
197	0.358750
198	0.359300
199	0.359850
200	0.360400

II. MODIFIED METHOD

The method for determining the number of millicuries to be administered to a patient so as to deliver a given centigray (cGy) dose to either the patient's lean body or the patient's total body set forth above may be modified. The following steps are involved according to the modified method of the present invention:

(1) Injecting a radioactive tracer into a patient;

(2) determining radiation levels in the whole body;

(3) calculating a geometric mean;

(4) determining the percent-injected activity remaining in the body at each time point;

(5) plotting the percent-injected activity versus calculated time from infusion on a log-linear graph;

(6) determining the effective half-life (and the rate of clearance) from the log-linear graph by identifying the intersection of the best fit line with the 50% injected activity line;

(7) cross-indexing the effective half-life value with the patient's body weight (either total body mass for total body dose or lean body mass for total body dose-lean) on either a graph or on a numerical chart to identify the actual amount of therapeutic millicuries per centigray [cGy] (delivered to total body mass or lean body mass); and

(8) multiplying the determined amount of therapeutic millicuries per centigray [cGy] (delivered to total body mass or lean body mass) by the amount of desired centigray (to total body mass or lean body mass) to be administered.

These steps along with their associated substeps are set forth in detail as follows and are to be read in correlation with the several figures discussed in conjunction therewith.

DETERMINATION OF RATE OF CLEARANCE

Determining the rate of clearance of an injected dose of a particular radiopharmaceutical is critical to the determination of the amount of therapeutic dose to be administered. A person who clears the injected dose quickly would receive a relatively large therapeutic dose of the particular radiopharmaceutical drug as compared to a person who clears the injected dose less quickly. This is simply because of residence time - the longer the radiopharmaceutical is proximate to the disease site, the less need be administered. Quick clearance translates into brief exposure to the radioactive element and less effective treatment of the disease. (Other factors determine the administered radioactivity dose, including the size of the patient and the desired total centigray amount.)

Rate of clearance according to the modified method of the present invention is determined by administering an amount of a "tracer dose" to the patient. The tracer dose represents a small amount of radioactivity attached to an antibody. As noted above, the methods of the present invention are not limited to use of an antibody. Rather, any protein or compound having specificity for a target cell or a target substance, provided the protein or compound is capable of carrying a radioactive marker or label, may be used according to the various methods disclosed herein.

The particular protein (such as an antibody) or compound (such as a phospholipidether) is selected according to its specificity to a target substance (such as an antigen) or to a target cell (such as a cancer cell). In light of the known utility of antibodies and by way of example, the following discussion will be based on the use of an antibody.

The "tracer dose" (in mCi) represents the amount of radioactivity that is initially administered to the patient. (The "tracer" aspect of this dose does not refer to a trace amount of antibody, but rather to the trace amount of radioactive material attached to the antibody. The antibody mass is delivered during the stage of estimating the rate of clearance in the same amount as in therapy, however, the amount of radioactivity administered is lower to prevent

toxicity to the system. Experimentation has shown that the tracer dose is, in fact, a reliable predictor of the therapeutic dose. Special measurements taken after therapy initially based upon a tracer dose has shown that the kinetics of clearance of the antibody with the tracer amount generally predict the kinetics of clearance of the therapeutic amount; in fact, these results are substantially identical.)

After administration of the tracer dose, the course of timing of the elimination of the tracer dose is thereafter followed. The tracer dose is first injected into the patient over a period of time, such as 40 minutes. Thereafter a probe is used to determine anterior and/or posterior counts, thus quantitatively demonstrating the amount of radioactivity remaining in the body after certain intervals of time. Measurements may be taken by any of several devices including a sodium-iodine probe, a gamma camera, a geiger counter, a whole-body counter, etc. Measurements are taken once approximately every 24 hours over a course of several days. Infusion stop and start times are recorded, as are counts taken for elimination over several 24-hour periods. The relevant intermediate numerical values are entered onto a worksheet such as that illustrated in Figure 3.

As an alternative to recording time points for each day of several days, as few as three (and possibly two) time points may be used to determine the shape and slope of the clearance curve of radioactivity from the body. This was verified through experimentation on twenty-eight patients who each received 700 mg total of anti-B-1 by comparing the dose calculated from eight time data points according to the computation methodology set forth above in the general method against the graphic-tabular approach and three time points of the modified method of the present invention. The comparative results are set forth in Figure 4. The correlation produced an r-value of 0.983 with a mean % difference in calculated mCi dose between the two methods being 3.33%. As illustrated in the accompanying Figure 4, the slope is 0.99 and the intercept is essentially 0. Accordingly, using the present graphic-

tabular method, three probe determinations taken at 0, 3, and 7 days may be used to calculate patient dose.

Once the counts are recorded over the requisite time period, the geometric mean is obtained. This may be done by taking readings from daily NaI probe measurements, but also may be done by relying upon readings from anterior and posterior conjugate view gamma camera imaging. When the latter approach is used, a geometric mean is obtained for each set of recorded anterior and posterior counts (representing an individual time point) is determined by the following formula:

$$\textbf{geometric mean} = \sqrt{\textbf{anterior count} \times \textbf{posterior count}}$$

The determined geometric mean is not corrected for radioactive decay. Once the geometric mean is known, net geometric mean counts are calculated by subtracting background counts according to the following formula:

$$\textbf{geometric mean (net)} = \textbf{geometric mean} - \textbf{bkg}$$

For example, if the background count is 100 cpm and the patient's count is 2000 cpm, then the net counts to the patient would be 1900 cpm.

Thereafter, the percent-injected activity remaining in the body at each time point is determined by forming a ratio to the geometric mean at the initial time point (again, not corrected for radioactive decay) according to the following:

$$\begin{array}{l}\textbf{percent-injected activity} \\ \textbf{(at each time point)}\end{array} = \frac{\textbf{geometric mean (net)}}{\textbf{geometric mean (initial)}} \times 100\%$$

Once the percent-injected activity for each time point is known, these values are entered into a graph to determine total body effective half life. Figure 5 is a blank graph consisting of a log linear graph onto which the pertinent values are to be marked. The percent-activity is read along the Y-

axis (log scale) and the time from injection (in hours) is read along the X-axis (linear scale).

Figure 6 is the graph of Figure 5 now completed and showing the relevant values of two patients. Patient "A" is denoted by a series of eight open boxes representing measurements of percent-injected activity recorded over a period of 160 hours. Patient "B" is denoted by a series of eight closed circles also representing measurements of percent injected activity recorded over the same period of time. Lines are drawn through the respective series of open boxes or closed circles to establish the respective curves.

The effective half-life for each patient is determined by identifying the point at which the respective curves intersect the 50% injected activity level, indicated by a horizontal line on the charts of both Figures 5 and 6. This point represents the effective half-life, or T 1/2-effective. Given, for example, Patient A, T 1/2-effective is 88 hours, while T 1/2-effective for Patient B is 47 hours. Obviously, Patient A clears the injected dose more slowly than does Patient B.

TOTAL BODY DOSE VERSUS TOTAL BODY DOSE-LEAN

The present invention improves on the known techniques of determining the optimal dose for administration of therapeutic radiopharmaceuticals in several ways. One such improvement rests in the unsettling of the previously-held notion that doses of therapeutic radiation could be determined based on patient weight. This notion fails to take into account several variables, including "fat" versus "lean" compartments and the related effects of "total body dose" versus "total body dose-lean".

The body represents two major compartments, a "fat" compartment and a "lean" compartment. The corollary to this is that the "lean" person resides within an outer shell of "fat". These related theories represent a major departure from other approaches to dosimetry. Accordingly, a calculation of the quantity of the patient which is "lean body mass" can be made. From this new mass and new shape which essentially isolates the "lean" from the "fat", a new and more accurate radiation dose can be determined to the "lean body"

using methods of least squares or graphical fitting of kinetic radioantibody clearance data and assumptions of non-uniform distribution of radioactivity between the two body compartments.

Figure 7 demonstrates the significance of distinguishing between "lean" and "fat" body compartments. Figure 7 is a "fused" image of a cross-section of a patient following administration of radiolabelled antibodies. The image is produced by a fusion computer program that superimposes a CT image slice corresponding to a SPECT image slice. Details of this procedure and its application are set forth in an article by K.F. Koral et al. and entitled CT-SPECT FUSION PLUS CONJUGATE VIEWS FOR DETERMINING DOSIMETRY IN IODINE-131-MONOCLONAL ANTIBODY THERAPY OF LYMPHOMA PATIENTS (J. Nucl. Med., Vol. 35, No. 10, October 1994, pps. 1714-1720). Generally, Figure 7 illustrates a central body compartment that includes the major organs such as the kidneys and spleen. The individual images are scaled by a computer so they substantially overlap when superimposed. The lighter areas are areas of relatively high amounts of radioactivity, while the darker areas are areas of low radioactivity.

With respect to Figure 7, a tumor, T, is shown in close association with the right kidney, labelled Rt K. Other organs illustrated include the aorta, A, the left kidney, Lf K, and the spleen, Sp. The patient's external body outline, labelled O, is illustrated, having thereupon a marker, M, to demonstrate the position of the body outline O. The outline O is the outer boundary of the patient and therefor represents the air-skin interface. The black area is mainly non-lean tissue, with the gray areas being the central area or the leaner body mass. As illustrated, there is a considerable amount of radioactivity in the vascular or lean component where antibody presence is the greatest. There is comparatively little radioactivity in the non-lean tissue, as illustrated by the black color. The patient illustrated in Figure 7 is a relatively large person having an excess amount of body fat. The body outline O would be closer to the internal organs on a thinner person.

While clearly illustrating the differences in uptake of the radiolabelled antibody between the lean and non-lean compartments, Figure 7 also demonstrates how it is generally not possible to target the disease site itself. While careful selection of a particular antibody will minimize cross-reaction with normal tissue, interaction (specific or non-specific) with non-disease tissue invariably results, in that as antibodies are directed to the tumor through blood vessels, the same vessels will naturally transport the antibodies in places other than to the disease site. Figure 7 also illustrates the simple assumption of the present invention that all (or substantially all) radioactivity resides in the "lean" compartment, while none (or virtually none) resides in the "fat" compartment, which encases the "lean" compartment. With the further assumption that the bone marrow is part of the freely accessible "lean" compartment, a beta particle dose and photon dose to the "lean" compartment can be determined. These estimations are important, in that the total amount of energy deposited in an individual as a result of radioactive decay is the "radiation dose" which is adjusted per unit weight for the particular individual or tissue and for a particular radioactive material. A specific example is the radioactive material I-131 which is both a beta emitter and a gamma emitter.

Following injection of an antibody labelled with I-131, for example, the central "lean" compartment of the body emits both beta and gamma particles. The beta particles are more or less confined within the compartment, while only some of the gamma particles are so confined. The extent to which the gamma particles are confined depends on the sizes of the "lean" and "fat" compartments. Some of the gamma particles strike some fat tissue and are scattered, returning to the "lean" compartment. Accordingly, not only does accurate quantification of the "lean" and "fat" compartments assist in eliminating reliance on the pure weight of a body in determining dose administration, an understanding of these compartments with respect to the individual patient also aids in determining, with greater accuracy, the "tracer dose" and its elimination.

Accordingly, it may now be understood that total body dose (TBD) assumes that all radioactivity is uniformly distributed throughout the patient's total body mass, and that all beta/electron energy is absorbed in the total body mass. TBD calculations for photon energy deposition are made from absorbed fractions of emissions of the radioactive material (for example, I-131) in the ellipsoid of mass equal to the total body mass. Conversely, total body dose - lean (TBD-Lean) is modeled as a lean-body mass ellipsoid surrounded by a fat-layer ellipsoid shell. TBD-Lean assumes that all radioactivity is uniformly distributed throughout the patient's lean body mass, since there is little tracer distribution to fat. In the TBD-Lean model, all beta/electron energy is absorbed in the lean-body mass, and photon energy is absorbed in lean-body mass ellipsoid volume. This said, it is clear that the more obese the patient, the more important dosage be based on the TBD-Lean model. Conversely, dosage for a relatively thin person could be reliably based on the TBD approach. However, regardless of the approach, the present method of determining optimal radiation dose could be used with either the TBD or the TBD-Lean model, with the latter model providing the better determination, particularly in the case of the obese patient.

Figure 8 illustrates the relationship of the fat component of the individual with respect to the lean component and accordingly is a visually simplified version of the actual section shown in Figure 7. An individual can be thought of as two ellipsoids, with the length x-1 or x-2 and with y-1 or y-2. The outer ellipsoid, labelled OE, with the larger x and y dimensions represents fat plus lean mass, with a volume (in liters) approximately equal to the patient's weight (in kilograms). The inner ellipsoid, labelled IE, with the same aspect ratios, is defined in liters by the following formulae that determine "lean body mass" (LBM):

$$45.5 + 0.91 \times (\text{height [in cm]} - 152) = \text{LBM for females}$$

$$48.0 + 1.06 \times (\text{height [in cm]} - 152) = \text{LBM for males}$$

It should be understood that total LBM could also be directly measured by CT, x-ray absorptiometry, immersion weighing, and other known methods. The

total body absorbed dose is then determined for the lean body ellipsoid based on the following methods. It should also be understood that corrections for Compton scatter of photons from the fat compartment or some trace accumulation in the fat compartment are also possible, but need to be included in the simplest application of the present method. Following this general guideline, the method of determining the patient's LBM of the above-described general method is followed.

DETERMINATION OF THE WHOLE BODY DOSE

With the effective half life or T 1/2-effective determined from tracer study, the whole body dose may be calculated. By "whole body dose", it is meant that these calculations are made for the whole body or for the lean body mass component of the whole body.

The calculations of the whole body dose according to the modified method are based on the assumption that the radioantibody is uniformly distributed throughout the patient (or the lean body mass compartment) following tracer injection and that the tissues are of uniform water density. Accordingly, determining the patient's mass (or lean body mass as set forth above) determines the assumed water content and patient volume for dosimetric calculations.

The "total body residence time" is an integral of the time activity curve for the total body divided by the injected activity according to the following formula:

The relative contributions of electron and photon radiation are summed to produce the total body radiation dose ([cGy]/mCi) administered. The formula for this determination is as follows, where the total body dose is the sum of

electron energy plus photon energy deposited in an ellipsoid having a mass m_{TB}:

This equation can be solved for A_T, the therapy activity in mCi to impart a given total body dose, D_{TB}.

These individual equations could be solved manually. However, it is preferred that the equations be reduced to graphical and tabular (numerical chart) formats, as illustrated in Figures 9a - 9p (for use in the graphical method) and Figures 10a - 10h (for use in the tabular method). A three-dimensional representation of the graphical method is illustrated in Figure 11. Such reductions greatly reduce the need for calculation and allow the method to be practiced without the need for complex computation.

To use the graphs of Figures 9a - 9p, the known effective half-life is cross-indexed with the patient's weight. The amount of therapeutic millicuries/cGy (for either total body dose or total body dose-lean) is set forth along the Y-axis, and the physician reads along the graph to the left to make this determination. To use the tables of Figures 10a - 10h, again the known effective half-life is cross-indexed with the patient's weight. The value at the intersection of the weight and T 1/2-effective is the amount of therapeutic millicuries/cGy.

Once the amount of therapeutic millicuries/cGy is established, this value is multiplied by the amount of desired centigray to be administered to treat a particular disease. These amounts are well known to those skilled in the art, but are not uncommonly in the 50-90 cGy range for whole-body dose.

Both the general and modified methods of the present invention may be more fully understood by reference to the following example.

EXAMPLE 2

A phase-I dose-escalation trial of I-131 labelled B1 antibody for the treatment of patients with non-Hodgkin's lymphoma was undertaken using a dose-escalation scheme designed around increasing levels of total body radiation dose. The overall results of the studies of 21 patients are set forth in the table of Figure 12. (The study began with 34 patients, hence the listing in the left-hand column of patient numbers with some patient numbers missing. Some of the missing patients, i.e., nos. 3, 11, 12, 17, 18, 20-23, 25, 26, 30, and 33, were bone marrow transplant patients or were patients who were subsequently not treated for various reasons, e.g., development of human antimouse antibody.)

Hematological toxicity was the major toxicity observed in the 21 patients studied that received radioimmunotherapy. Patients were treated with radioimmunotherapy doses calculated from tracer dosimetry studies (NaI probe) to deliver doses to the whole body ranging from 25 to 85 cGy. Hematological toxicity after treatment was assessed by the NCI common criteria, grades 0-4. Nine patients had no toxicity, 5-grade-1, 3-grade-2, 2-grade-3, and 2-grade-4 (grade 4 is the most severe). Total body dose was estimated by modeling the patient as a uniform activity distribution in an ellipsoid for the purpose of calculating the energy absorbed fraction of photons from I-131 decay. The parameter of the present invention, the Total Body Dose-Lean was introduced to account for the fact that obese patients can be modeled as an outer shell of fat (with little radioantibody accumulation) surrounding the active lean body mass. Irradiation of the fat layer would presumably have little effect on hematologic toxicity. Blood clearance and dose was determined from actual tracer blood samples. Marrow residence time was estimated using the assumption that specific activity in marrow is 30% of the specific activity in blood. Resulting correlation between estimated dose parameters from the tracer studies and hematological toxicity grade were as follows:

Dose Parameter	r-value	p-value (N=21)
blood-dose	0.337	0.146
marrow-dose	0.421	0.064
mCi/kg	0.270	0.236
TBD	0.430	0.052
TBD-lean	0.523	0.015

The TBD-lean correlated best with resulting toxicity following radioimmunotherapy in this patient group, offering a clear improvement over estimates of blood, marrow or TB dose.

The improvement according to the present invention is clearly observable by reference to the graphs of Figures 13 through 15. With respect first to the graph of Figure 13, dosage based on simple mCi per Kg of patient weight is set forth. The toxicity level correlates poorly with mCi/Kg due to the assumption of uniform distribution in the patient's total body mass, and also clearance kinetics are not taken into account. Figure 14 discloses a graph similar to that of Figure 13, but based upon total body dose (TBD) [cGy]. As illustrated, the toxicity grade from the administered dose correlates better with TBD than for the less exact method that produced the graph of Figure 13. Finally, Figure 15 discloses a graph similar to those of Figures 13 and 14, but illustrating results produced from reliance on the total body dose-lean (TBD-Lean) [cGy] method. The grade of toxicity from the administered dose is best predicted by the TBD-Lean method than that for the method based on total body dose (shown in Figure 14) and also the method based simply on mCi/body weight (shown in Figure 13).

Those skilled in the art can now appreciate from the foregoing description that the broad teachings of the present invention can be implemented in a variety of forms. Therefore, while this invention has been described in connection with particular examples thereof, the true scope of the invention should not be so limited since other modifications will become apparent to the skilled practitioner upon a study of the drawings, specification and following claims.

WHAT IS CLAIMED IS:

1. A method of establishing the optimal effective radiation dose in mCi for treatment of disease in a patient, said method comprising the steps of:

establishing the rate of clearance of a tracer dose from the patient's body;

identifying the effective half-life value of said tracer dose in the patient based on said rate of clearance;

determining the actual amount of therapeutic mCi per cGy based on the effective half-life of said tracer; and

multiplying said actual amount of therapeutic mCi per cGy by the amount of desired cGy to be administered.

2. The method of establishing the optimal effective radiation dose of Claim 1, including the further step of determining said actual amount of therapeutic mCi by cross-indexing said effective half-life value with the patient's body weight.

3. The method of establishing the optimal effective radiation dose of Claim 2, including the further step of cross-indexing said effective half-life value with the patient's total body mass for a total body dose.

4. The method of establishing the optimal effective radiation dose of Claim 2, including the further step of cross-indexing said effective half-life value with the patient's lean body mass for a total body dose-lean.

5. The method of establishing the optimal effective radiation dose of Claim 1, including the further steps of injecting a radioactive tracer into the patient and determining a radiation level for said injected radioactive tracer.

6. The method of establishing the optimal effective radiation dose of Claim 5, including the further step of calculating a geometric mean based on said determined radiation level.

7. The method of establishing the optimal effective radiation dose of Claim 6, wherein said geometric mean is based upon NaI probe measurements.

8. The method of establishing the optimal effective radiation dose of Claim 6, wherein said geometric mean is based upon anterior or posterior conjugate view gamma camera imaging data.

9. The method of establishing the optimal effective radiation dose of Claim 1, including the further step of determining the percent-injected activity remaining in the patient's body across a plurality of time intervals.

10. The method of establishing the optimal effective radiation dose of Claim 9, including the further step of plotting said percent-injected activity versus calculated elimination time from infusion on a log-linear graph.

11. The method of establishing the optimal effective radiation dose of Claim 10, wherein said log-linear graph includes a 50% injected activity line, said method including the further step of determining said effective half-life from said log-linear graph by identifying the intersection of the best fit line with said 50% injected activity line.

12. The method of establishing the optimal effective radiation dose of Claim 1, including the further step of cross-indexing said effective half-life with the patient's body weight on a graph having a first axis and a second axis substantially perpendicular to said first axis, said first axis having increments of Rx mCi/cGy and said second axis having increments of body mass to identify the actual amount of therapeutic mCi.

13. The method of establishing the optimal effective radiation dose of Claim 1, including the further step of cross-indexing said effective half-life with the patient's body weight on a table having a first axis and a second axis substantially perpendicular to said first axis, said first axis having increments of body mass and said second axis having increments of effective half-life to identify the actual amount of therapeutic mCi.

14. A method of establishing the optimal effective radiation dose for treatment of disease in a patient, said method comprising the steps of:

establishing the rate of clearance of a tracer dose from the patient's body;

identifying a numerical value based on said rate of clearance;

determining the actual amount of therapeutic mCi per cGy based on said numerical value by cross-indexing said numerical value with the patient's body weight; and

multiplying said actual amount of therapeutic mCi per cGy by the desired amount of cGy to be administered.

15. The method of establishing the optimal effective radiation dose of Claim 14, including the further step of identifying the effective half-life value of said tracer dose in the patient based on said rate of clearance.

16. The method of establishing the optimal effective radiation dose of Claim 15, including the further step of determining said actual amount of therapeutic mCi by cross-indexing said effective half-life value with the patient's body weight.

17. The method of establishing the optimal effective radiation dose of Claim 16, including the further step of cross-indexing said effective half-life value with the patient's total body mass for a total body dose.

18. The method of establishing the optimal effective radiation dose of Claim 17, including the further step of cross-indexing said effective half-life value with the patient's lean body mass for a total body dose-lean.

19. A method of establishing the optimal effective radiation dose for treatment of disease in a patient, said method comprising the steps of:

identifying the effective half-life value of a tracer in the patient; and

determining the actual amount of therapeutic mCi based on the effective half-life of said tracer.

20. The method of establishing the optimal effective radiation dose of Claim 19, including the further step of multiplying said actual amount of therapeutic mCi per cGy by the amount of desired cGy to be administered.

21. The method of establishing the optimal effective radiation dose of Claim 1, wherein said step of determining the actual amount of therapeutic mCi per cGy is also based on the patient's total body mass.

22. The method of establishing the optimal effective radiation dose of Claim 1, wherein said step of determining the actual amount of therapeutic mCi per cGy is also based on the patient's lean body mass.

23. A method of establishing the optimal effective radiation dose in mCi for treatment of disease in a patient, said method comprising the steps of:

establishing the rate of clearance of a tracer dose from the patient's body;

identifying the effective half-life value of said tracer dose in the patient based on said rate of clearance;

determining the actual amount of therapeutic mCi per cGy based on the effective half-life of said tracer;

multiplying said actual amount of therapeutic mCi per cGy by the amount of desired cGy to be administered; and

administering the radiation dose.

24. Use of an apparatus for establishing the optimal effective radiation dose in mCi for treatment of disease in a life form comprising means for establishing the rate of clearance of a tracer dose from the life form, means for identifying the effective half-life value of said tracer dose in the life form based on said rate of clearance, means for determining the actual amount of therapeutic mCi per cGy based on the effective half-life of said tracer, and means for multiplying said actual amount of therapeutic mCi per cGy by the amount of desired cGy to be administered.

25. An apparatus for establishing the optimal effective radiation dose in mCi for treatment of disease in a patient, said apparatus comprising:

means for establishing the rate of clearance of a tracer dose from the patient's body;

means for identifying the effective half-life value of said tracer dose in the patient based on said rate of clearance;

means for determining the actual amount of therapeutic mCi per cGy based on the effective half-life of said tracer; and

means for multiplying said actual amount of therapeutic mCi per cGy by the amount of desired cGy to be administered.

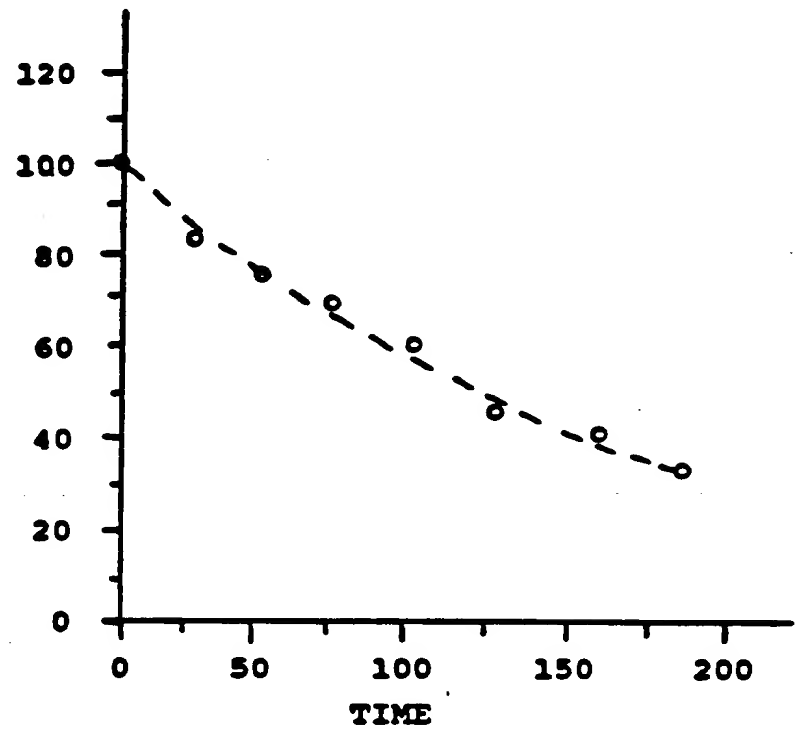

Fig. 2

Integ. to last data point=
2882.67 [%]131-hr]

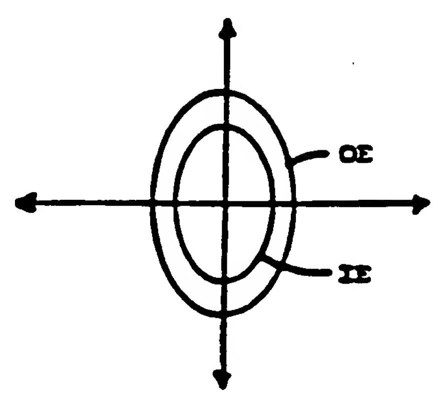

Fig. 1

Fig. 3

Diagnostic Total Body Clearance

Patient: ______________

Infusion Date/time: ______________

Injected activity: __________ mCi

Patient Lean Body (or Total Body) mass: __________ Kg

Projected TB-lean (or TB) dose: __________ cGy

nominal time point	time post infusion [hrs]	anterior whole body	posterior whole body	background	GM	GMnet	%injected activity
immed post infusion							
1 day post							
2 day post							
3 day post							
4 day post							
5 day post							
6 day post							
7 day post							

Effective half life: __________ hrs

A0 (from table lookup): __________ mCi/cGy

Prescribed therapy activity (for TBdose-lean or TBdose) = A0 * Projected TB-lean dose: __________ mCi

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Fig. 4

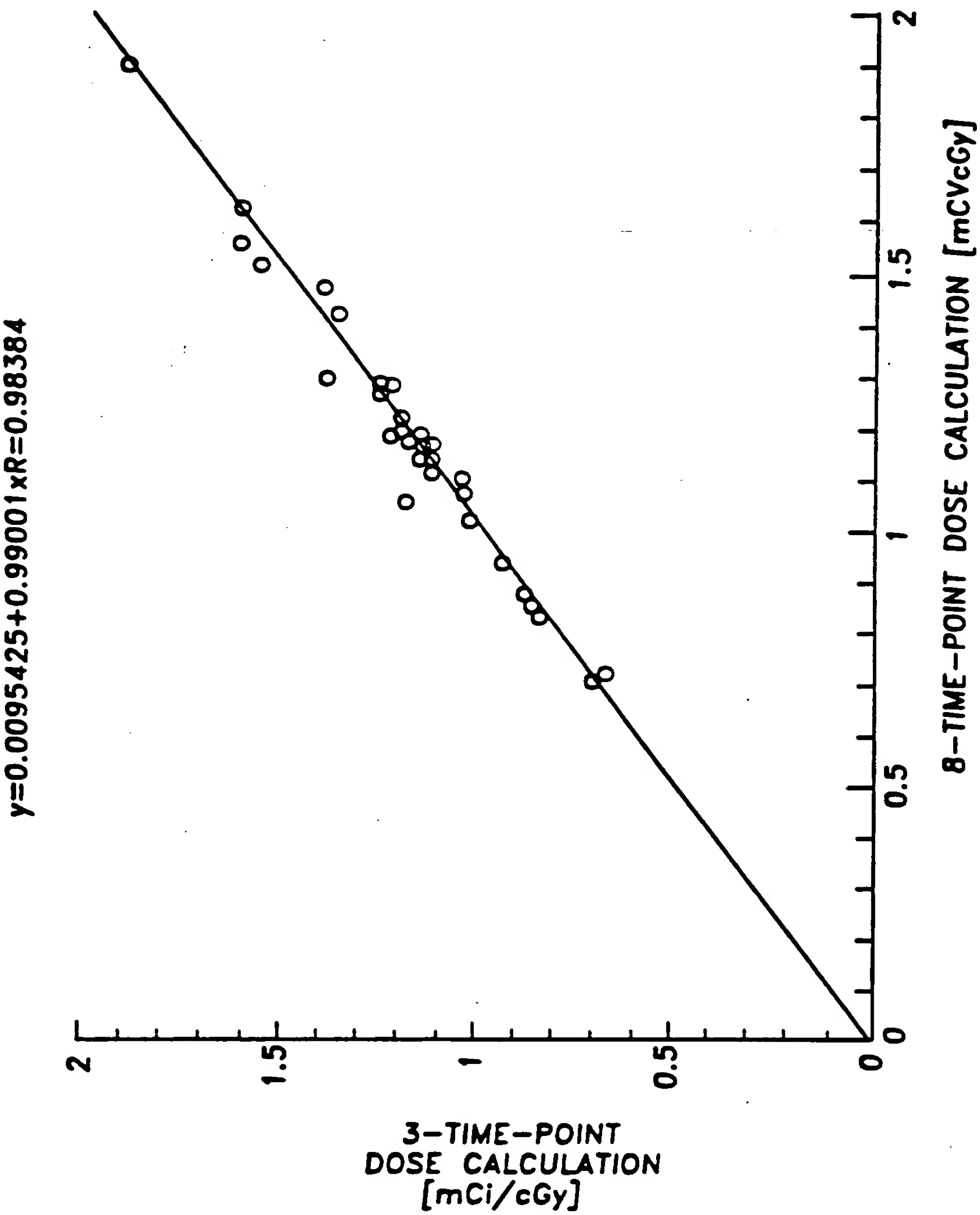

y=0.0095425+0.99001xR=0.98384
8-TIME-POINT DOSE CALCULATION [mCVcGy]
3-TIME-POINT DOSE CALCULATION [mCi/cGy]
0
0.5
1
1.5
2

Fig. 5

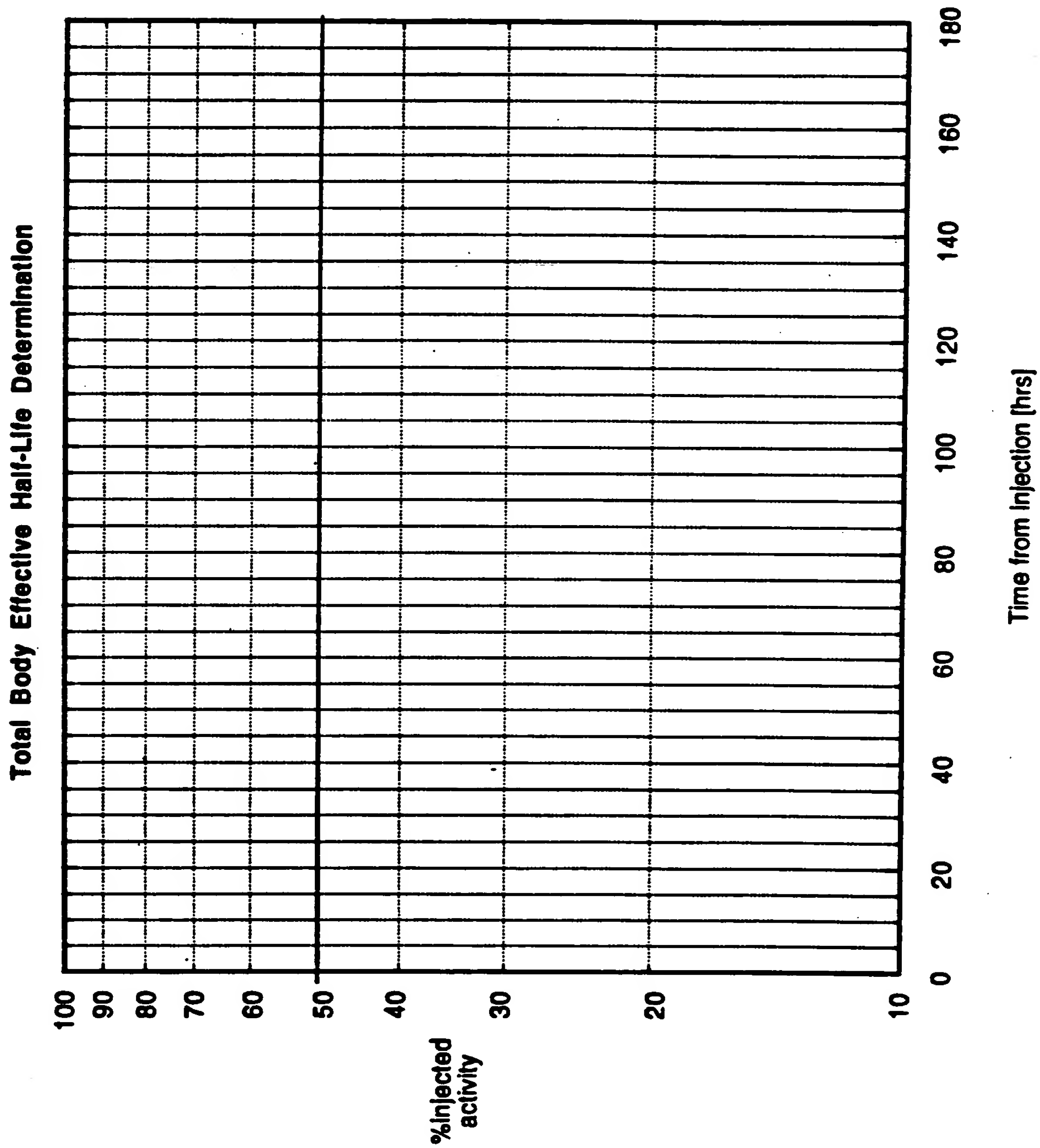
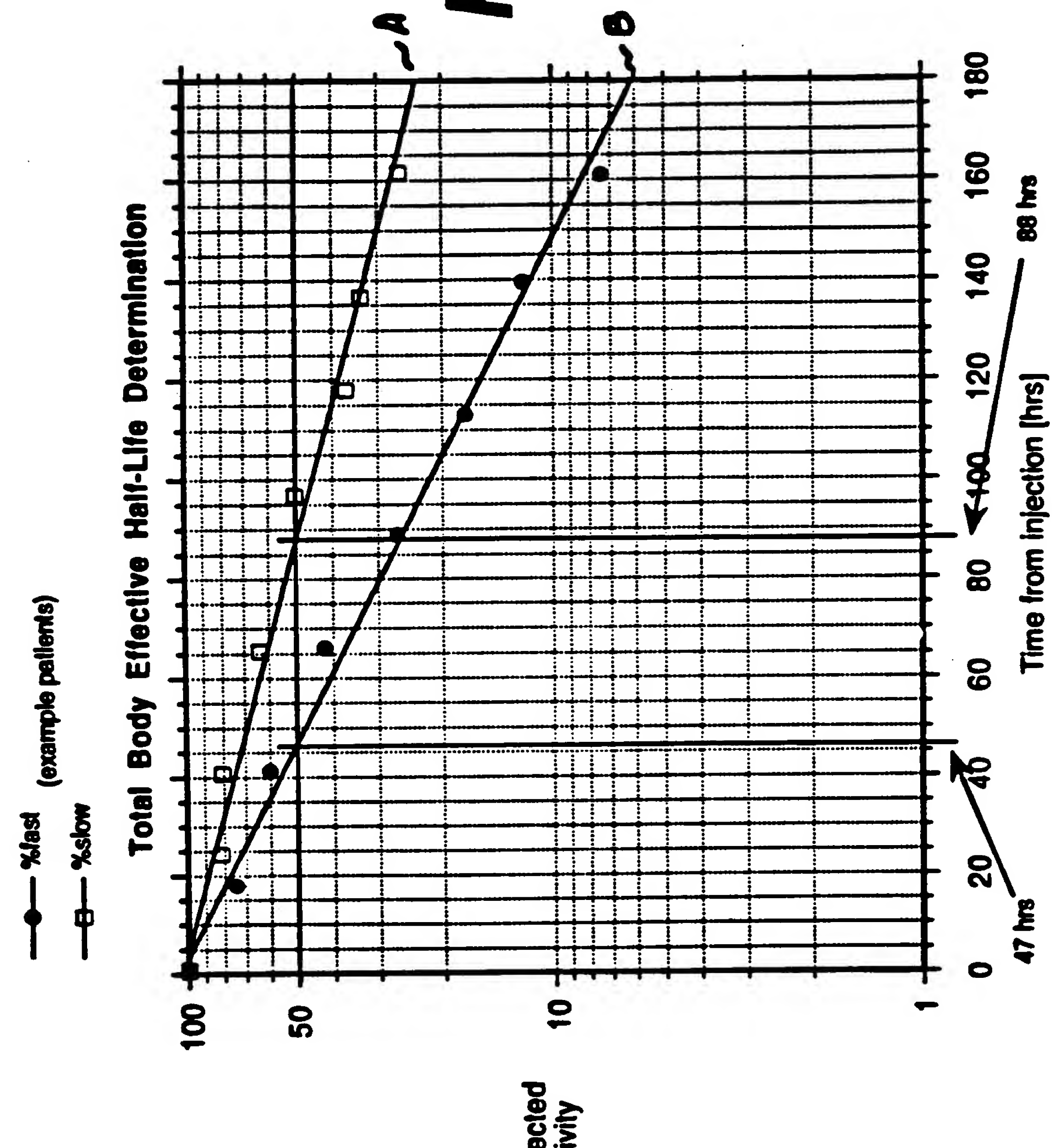

Total Body Effective Half-Life Determination
%injected activity
100
90
80
70
60
50
40
30
20
10
0
20
40
60
80
100
120
140
160
180
Time from Injection [hrs]

Fig. 6


Total Body Effective Half-Life Determination
%fast
%slow
(example patients)
%injected activity
100
50
10
1
0
20
40
60
80
100
120
140
160
180
Time from injection [hrs]
47 hrs
88 hrs
A
B

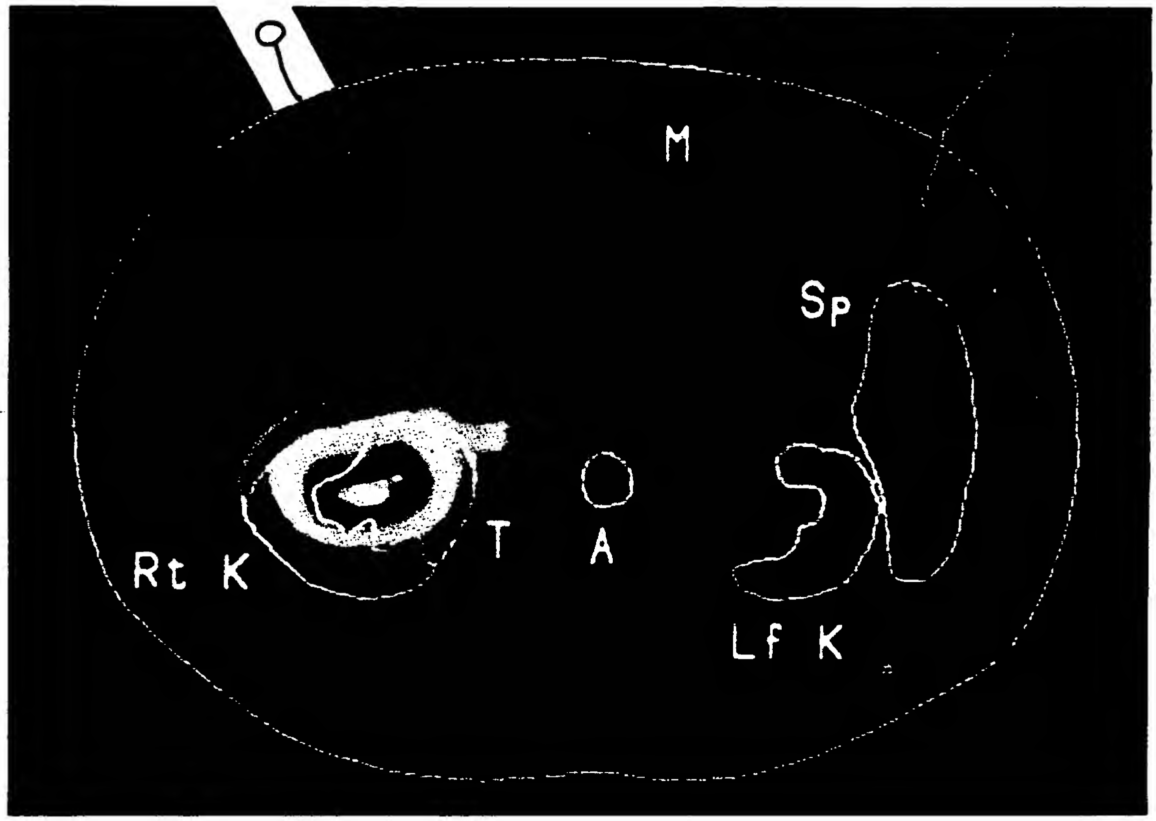


Fig. 7

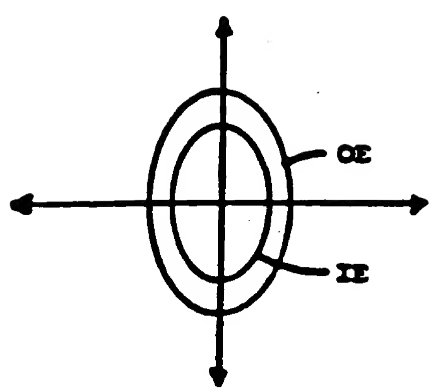


Fig. 8

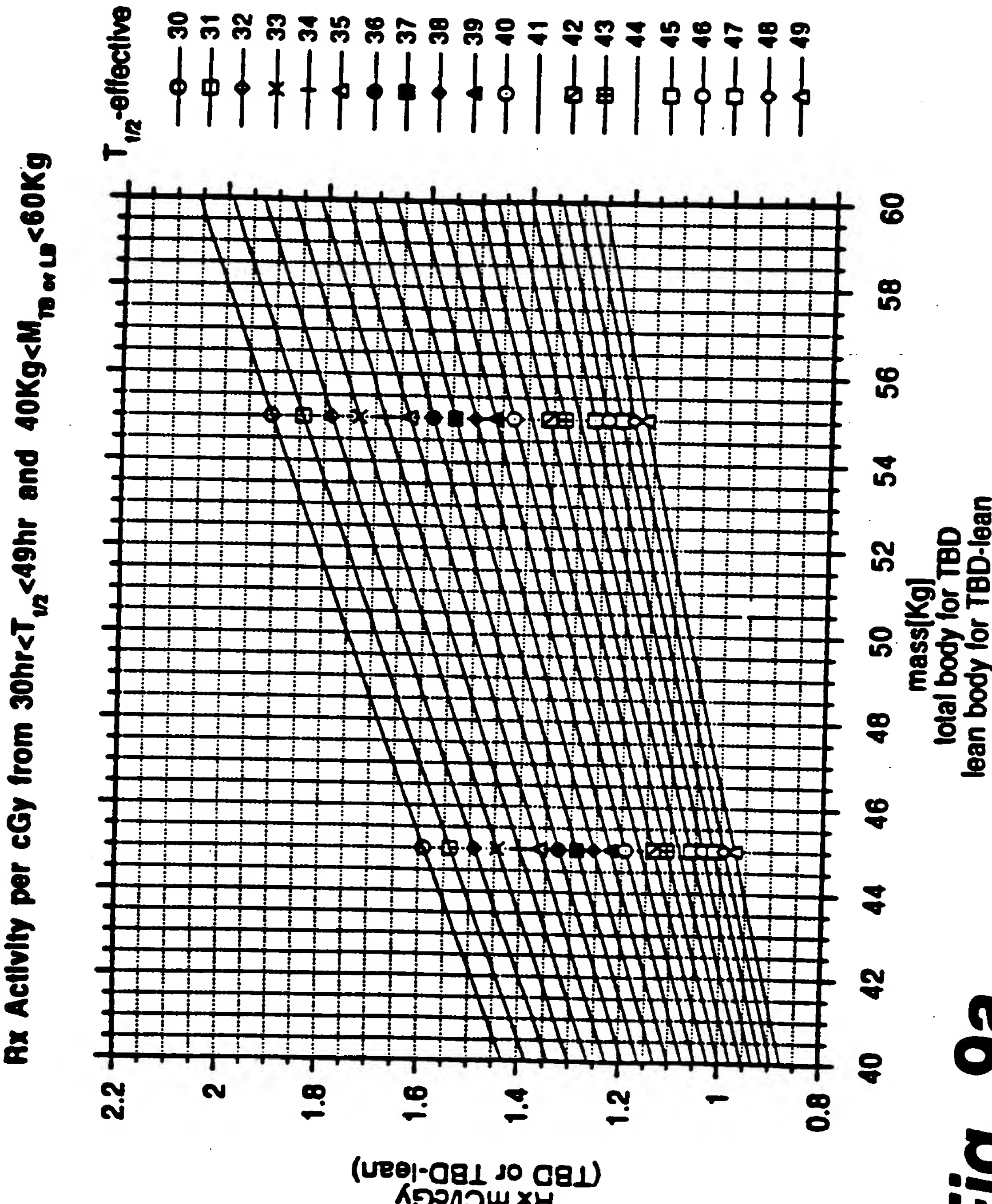

Rx Activity per cGy from 30hr<T1/2<49hr and 40Kg<M TB or LB <60Kg
T1/2-effective
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
Rx mCi/cGy
(TBD or TBD-lean)
2.2
2
1.8
1.6
1.4
1.2
1
0.8
40
42
44
46
48
50
52
54
56
58
60
mass[Kg]
total body for TBD
lean body for TBD-lean

Fig. 9a

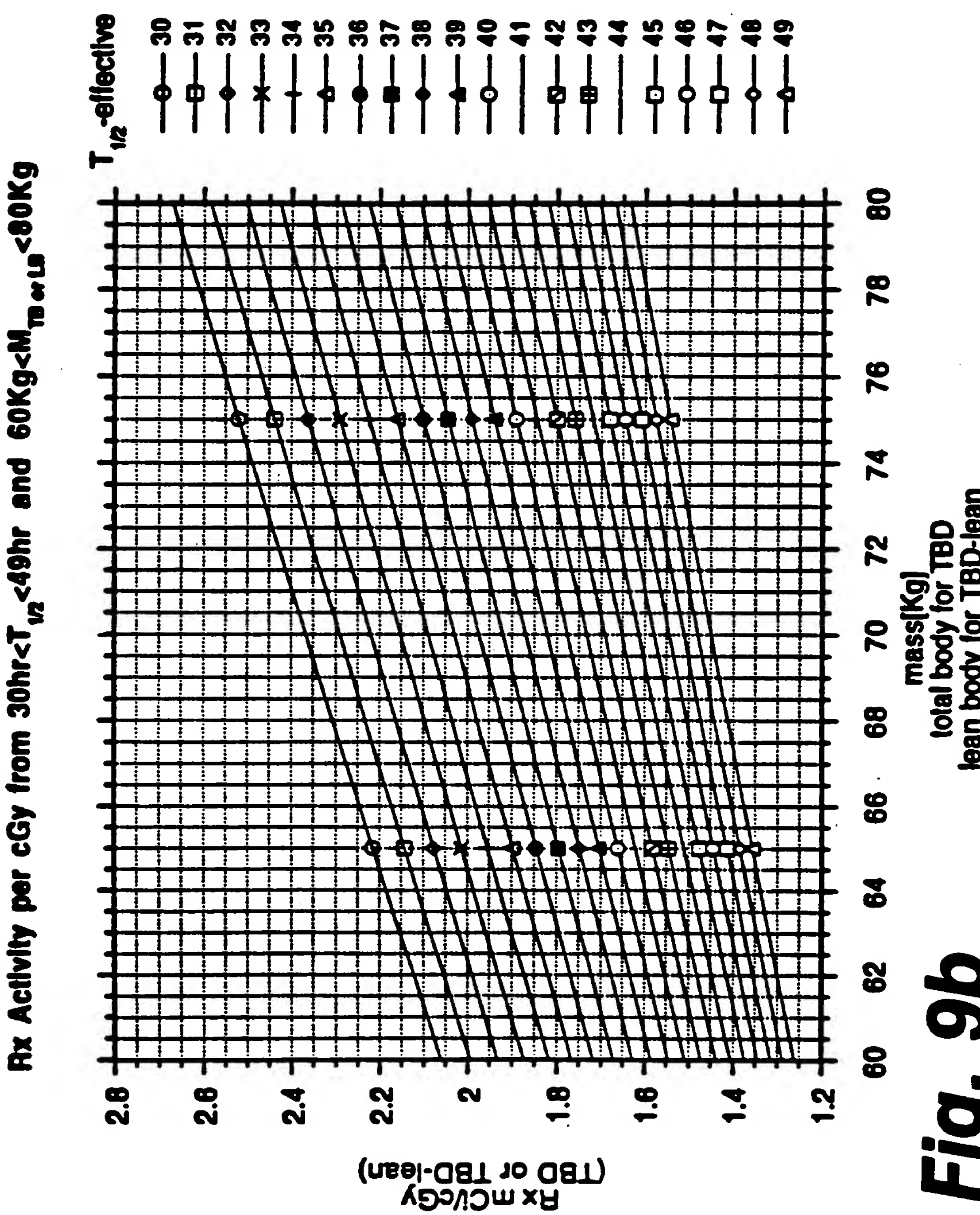
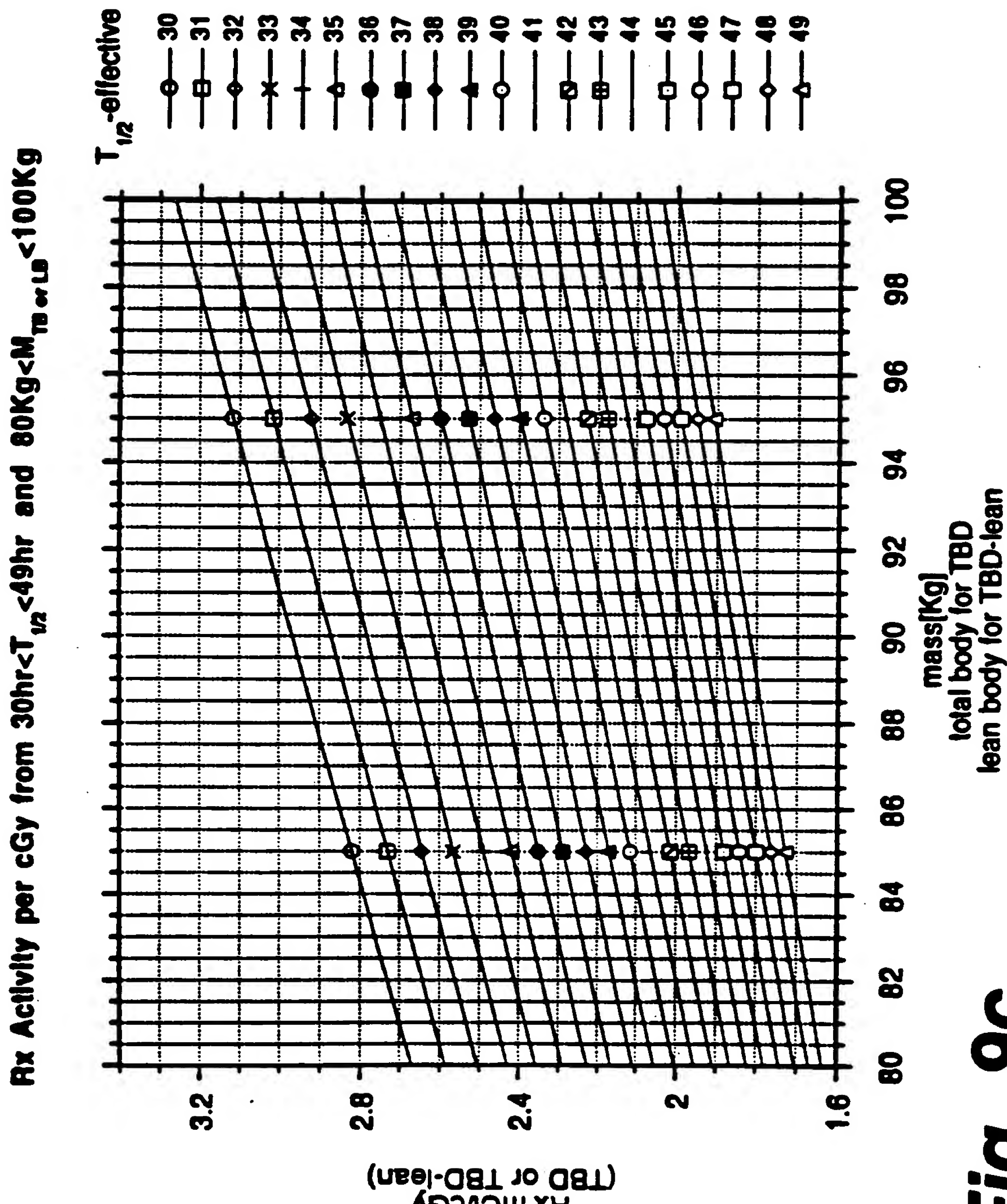

Rx Activity per cGy from 30hr<T1/2<49hr and 60Kg<MTB or LB<80Kg
T1/2-effective
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
Rx mCi/cGy
(TBD or TBD-lean)
2.8
2.6
2.4
2.2
2
1.8
1.6
1.4
1.2
60
62
64
66
68
70
72
74
76
78
80
mass[Kg]
total body for TBD
lean body for TBD-lean

Fig. 9b



Rx Activity per cGy from 30hr<T1/2<49hr and 80Kg<M TB or LB<100Kg
T1/2-effective
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
Rx mCi/cGy (TBD or TBD-lean)
3.2
2.8
2.4
2
1.6
80
82
84
86
88
90
92
94
96
98
100
mass[Kg]
total body for TBD
lean body for TBD-lean

Fig. 9c

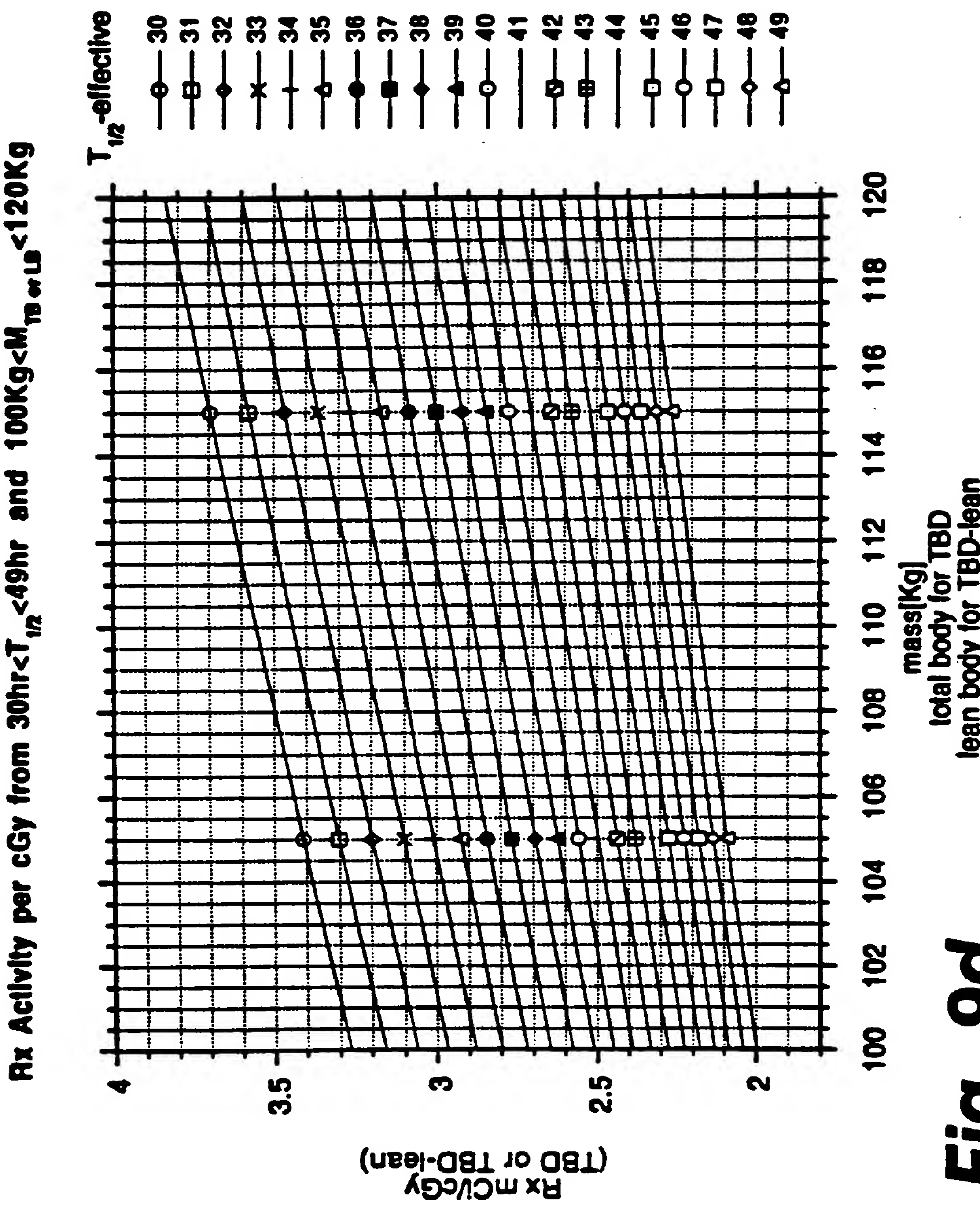

Rx Activity per cGy from 30hr<T1/2<49hr and 100Kg<M TB or LB<120Kg
T1/2-effective
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
Rx mCi/cGy
(TBD or TBD-lean)
4
3.5
3
2.5
2
100
102
104
106
108
110
112
114
116
118
120
mass[Kg]
total body for TBD
lean body for TBD-lean

Fig. 9d

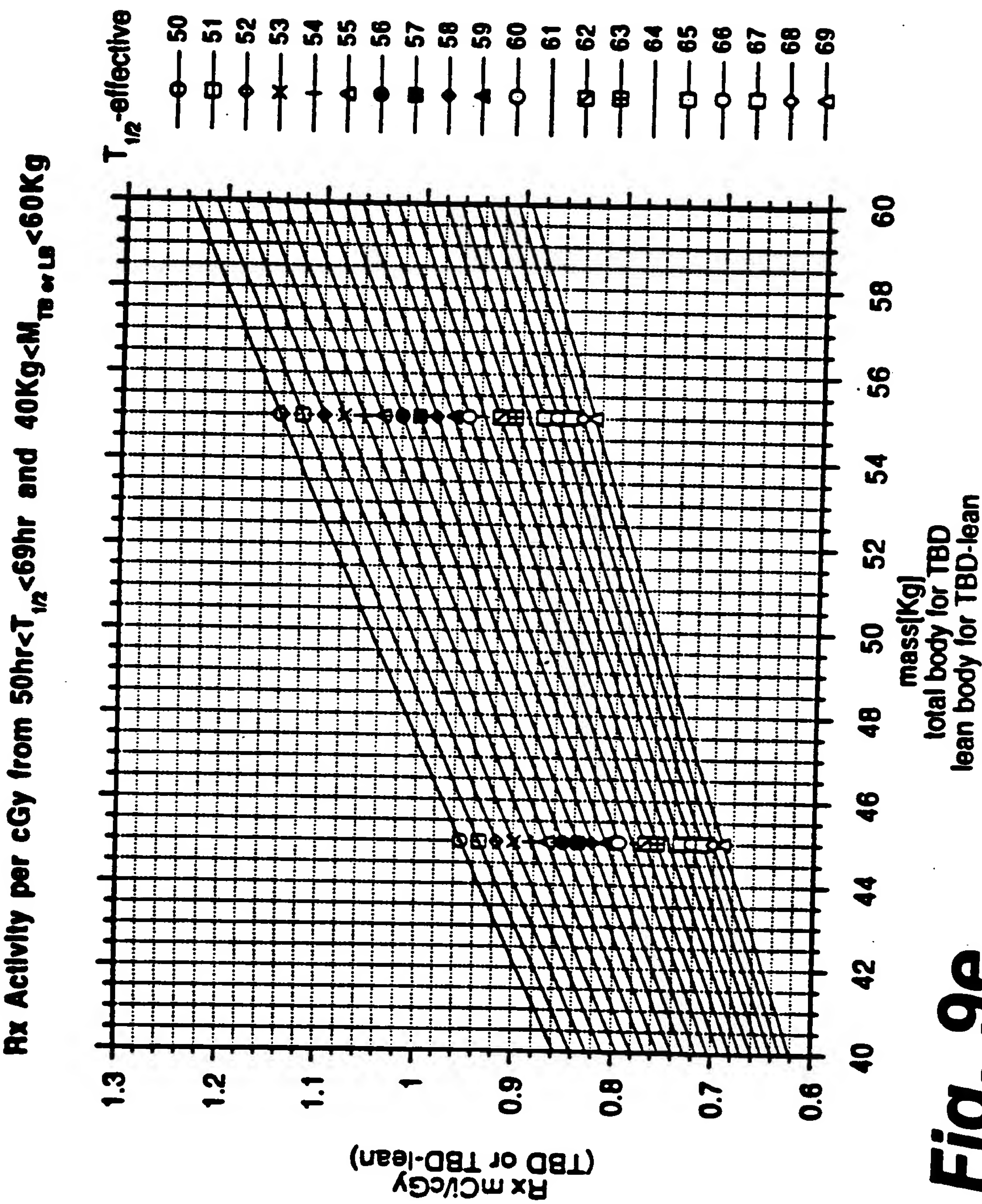
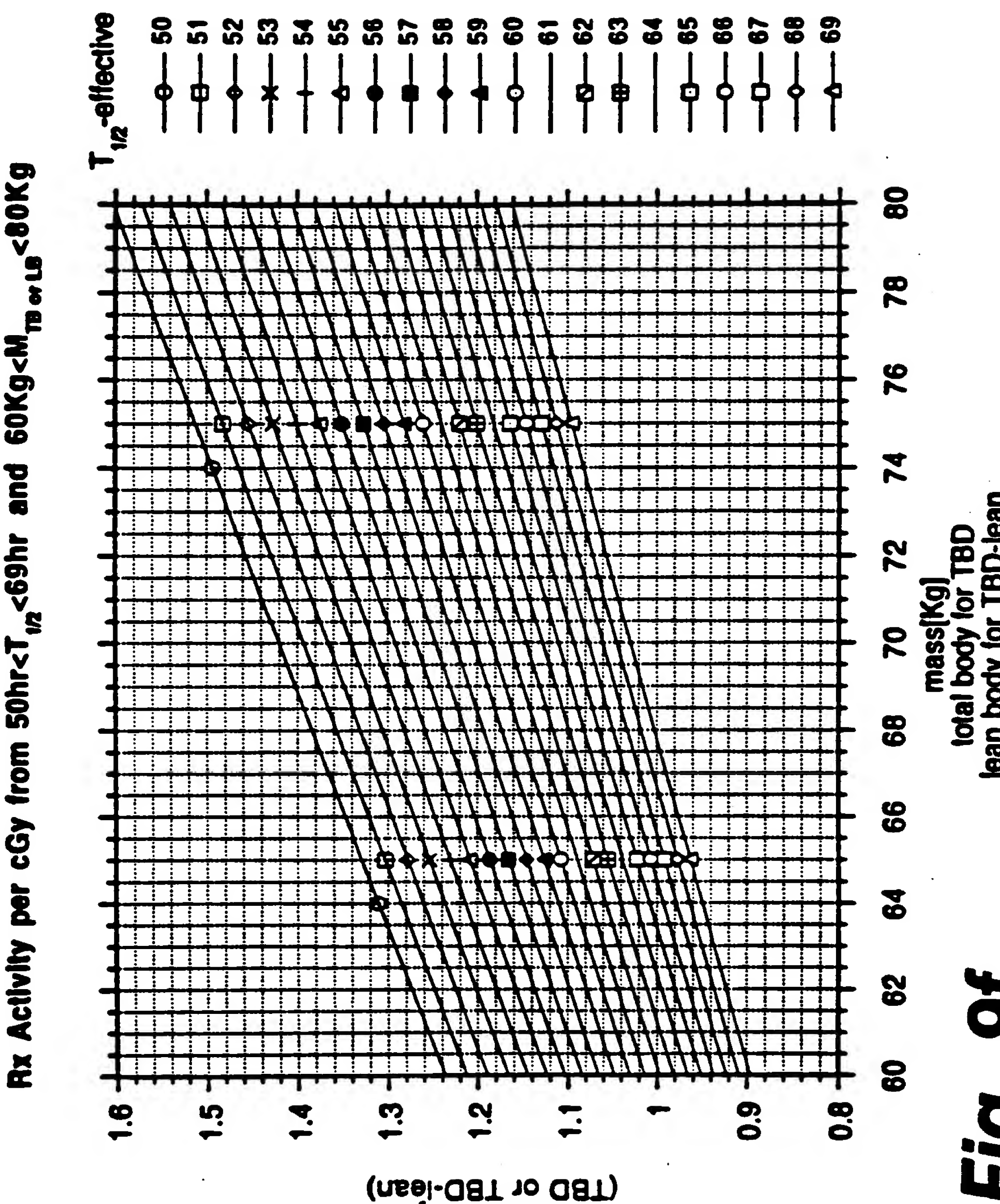

Rx Activity per cGy from 50hr<T1/2<69hr and 40Kg<M TB or LB<60Kg
T1/2-effective
50
51
52
53
54
55
56
57
58
59
60
61
62
63
64
65
66
67
68
69
Rx mCi/cGy
(TBD or TBD-lean)
1.3
1.2
1.1
1
0.9
0.8
0.7
0.6
40
42
44
46
48
50
52
54
56
58
60
mass[Kg]
total body for TBD
lean body for TBD-lean

Fig. 9e



Rx Activity per cGy from 50hr<T1/2<69hr and 60Kg<M TB or LB<80Kg
T1/2-effective
50
51
52
53
54
55
56
57
58
59
60
61
62
63
64
65
66
67
68
69
Rx mCi/cGy
(TBD or TBD-lean)
1.6
1.5
1.4
1.3
1.2
1.1
1
0.9
0.8
60
62
64
66
68
70
72
74
76
78
80
mass[Kg]
total body for TBD
lean body for TBD-lean

Fig. 9f

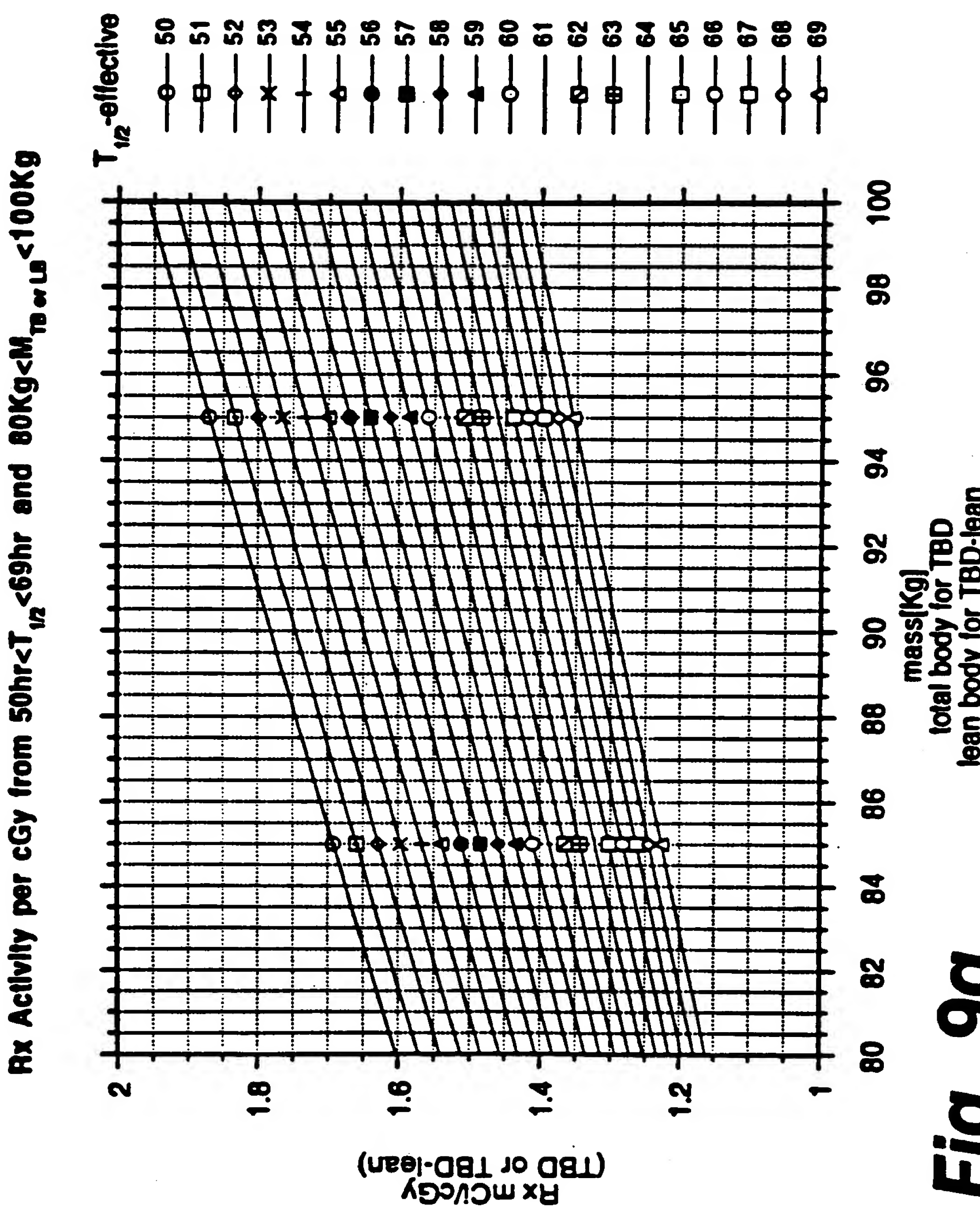

Rx Activity per cGy from 50hr<T1/2<69hr and 80Kg<MTB or LB<100Kg
T1/2-effective
50
51
52
53
54
55
56
57
58
59
60
61
62
63
64
65
66
67
68
69
Rx mCi/cGy
(TBD or TBD-lean)
2
1.8
1.6
1.4
1.2
1
80
82
84
86
88
90
92
94
96
98
100
mass[Kg]
total body for TBD
lean body for TBD-lean

Fig. 9g

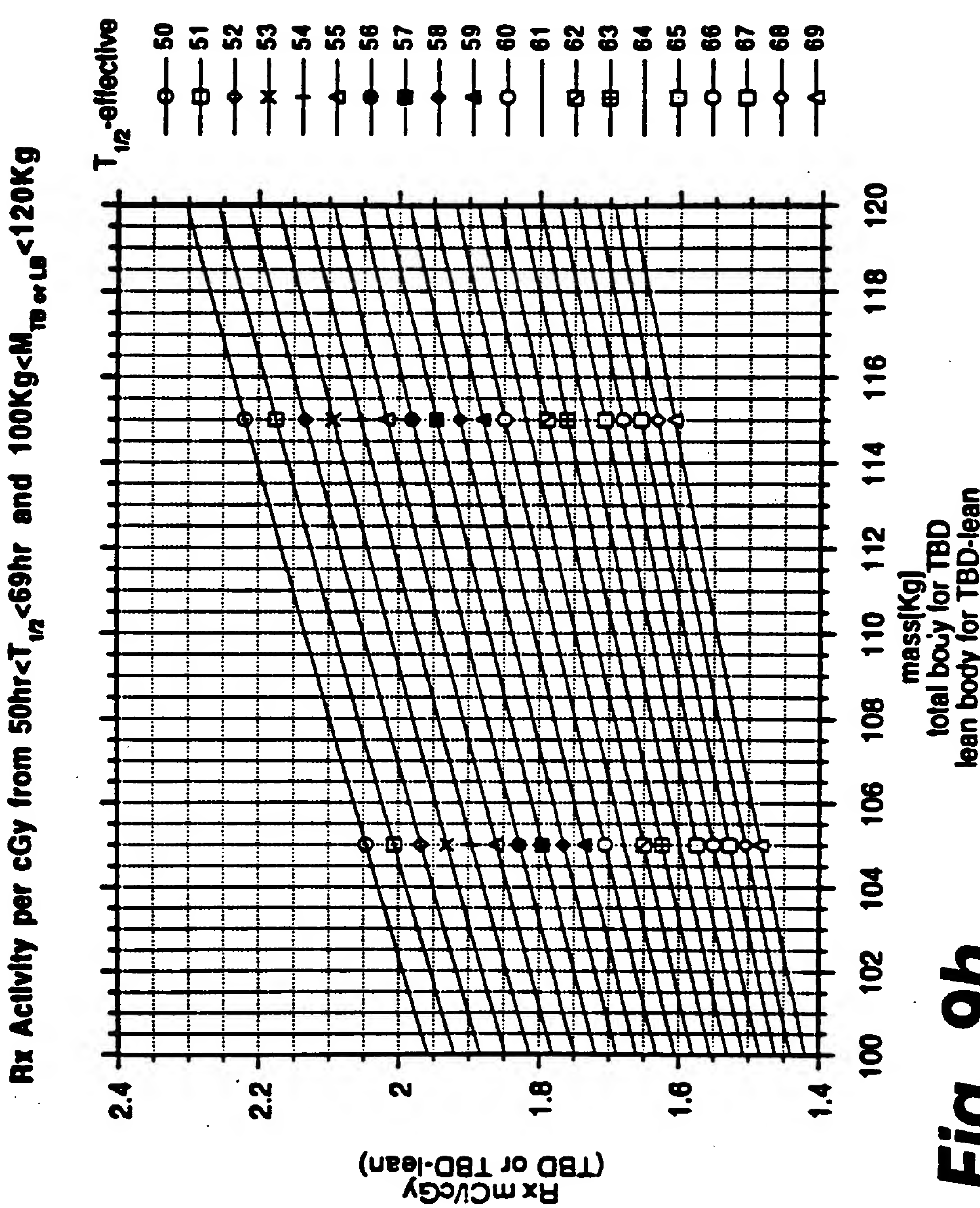

Rx Activity per cGy from 50hr<T1/2<69hr and 100Kg<M TB or LB<120Kg
T1/2-effective
50
51
52
53
54
55
56
57
58
59
60
61
62
63
64
65
66
67
68
69
Rx mCi/cGy
(TBD or TBD-lean)
2.4
2.2
2
1.8
1.6
1.4
100
102
104
106
108
110
112
114
116
118
120
mass[Kg]
total body for TBD
lean body for TBD-lean

Fig. 9h

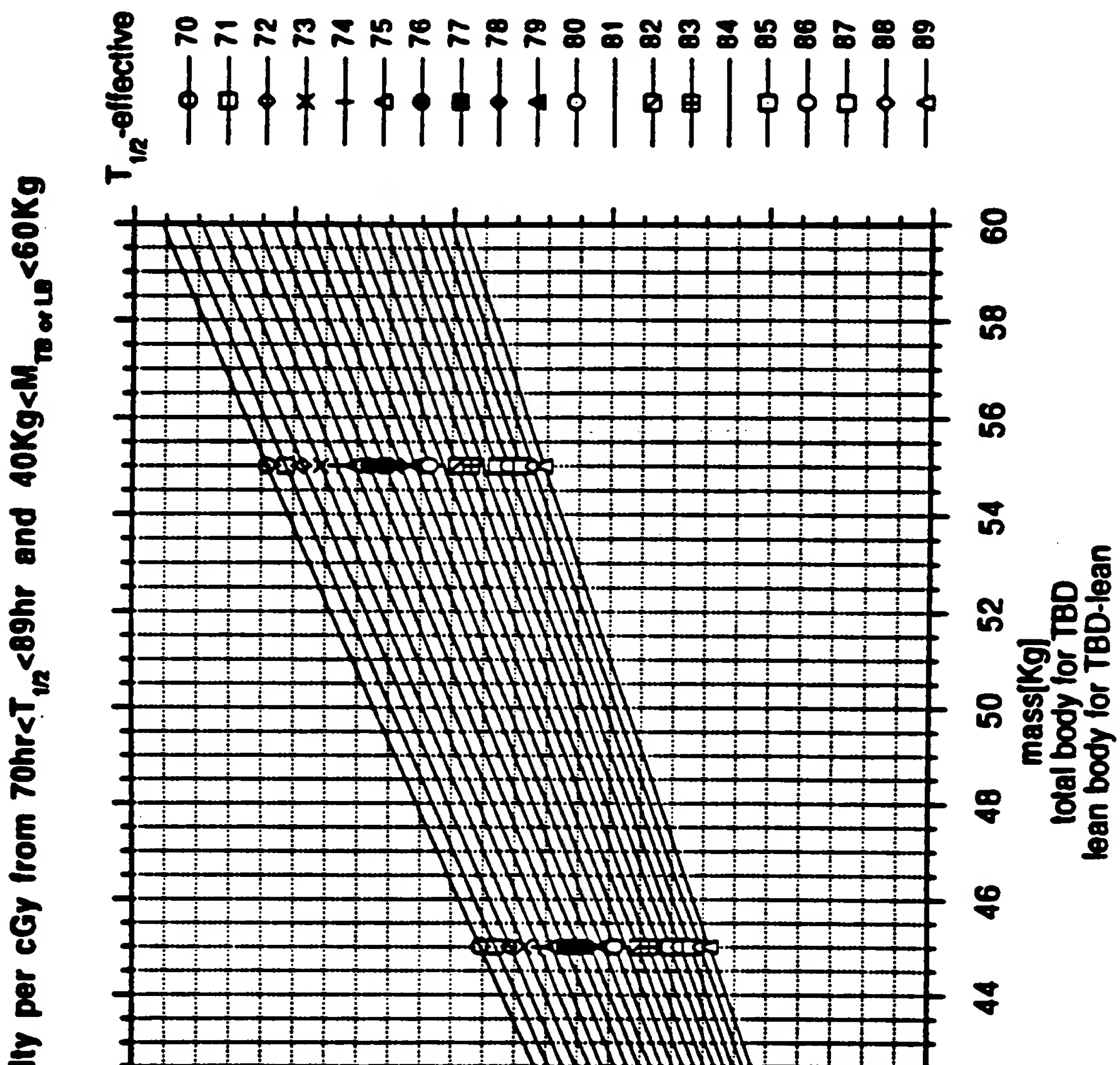

Rx Activity per cGy from 70hr<$T_{1/2}$<89hr and 40Kg<$M_{TB\ or\ LB}$<60Kg
$T_{1/2}$-effective
70
71
72
73
74
75
76
77
78
79
80
81
82
83
84
85
86
87
88
89
Rx mCi/cGy
(TBD or TBD-lean)
0.9
0.8
0.7
0.6
0.5
0.4
40
42
44
46
48
50
52
54
56
58
60
mass[Kg]
total body for TBD
lean body for TBD-lean

Fig. 9i

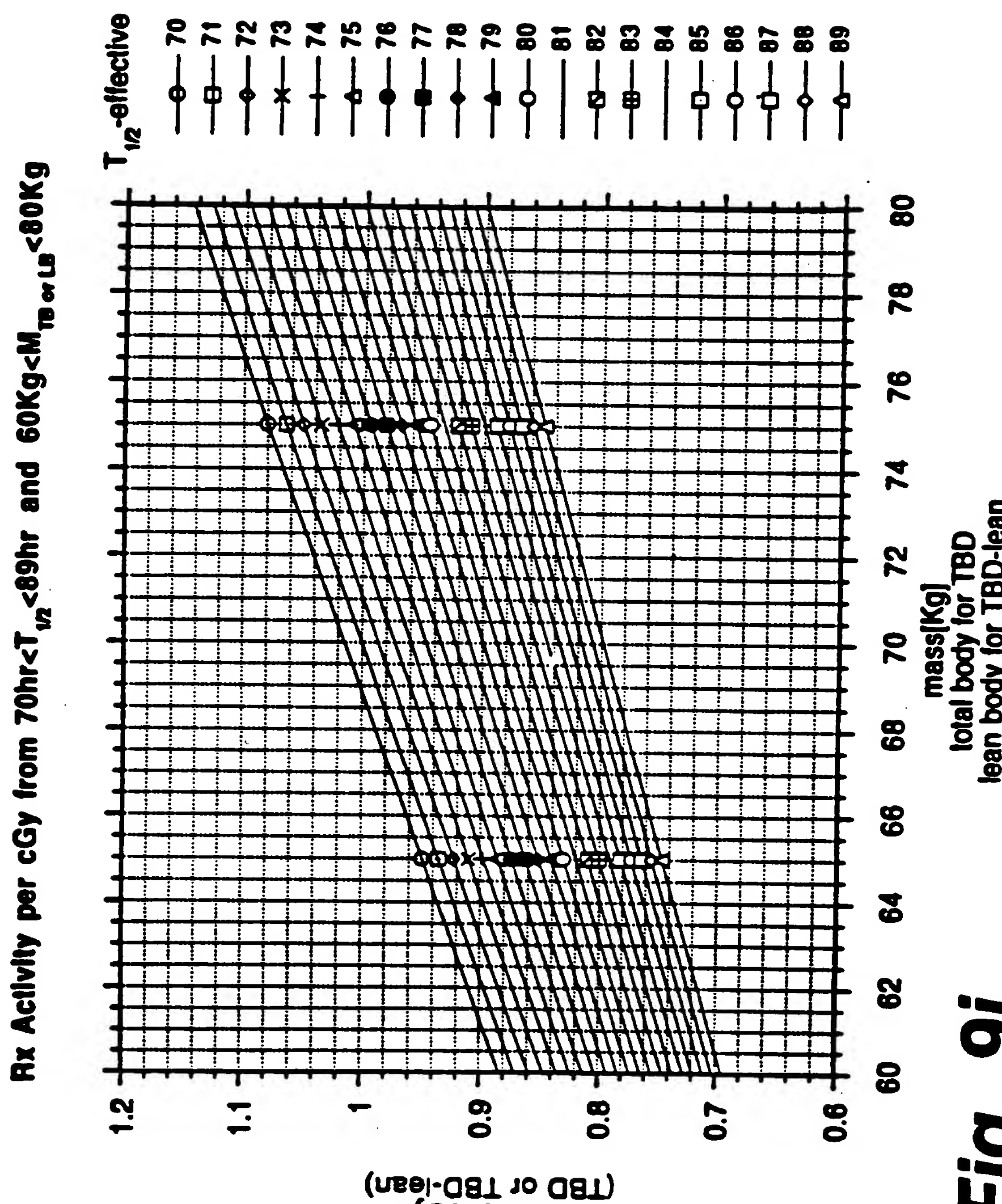

Rx Activity per cGy from 70hr<T1/2<89hr and 60Kg<MTB or LB<80Kg
T1/2-effective
70
71
72
73
74
75
76
77
78
79
80
81
82
83
84
85
86
87
88
89
Rx mCi/cGy
(TBD or TBD-lean)
1.2
1.1
1
0.9
0.8
0.7
0.6
60
62
64
66
68
70
72
74
76
78
80
mass[Kg]
total body for TBD
lean body for TBD-lean

Fig. 9j

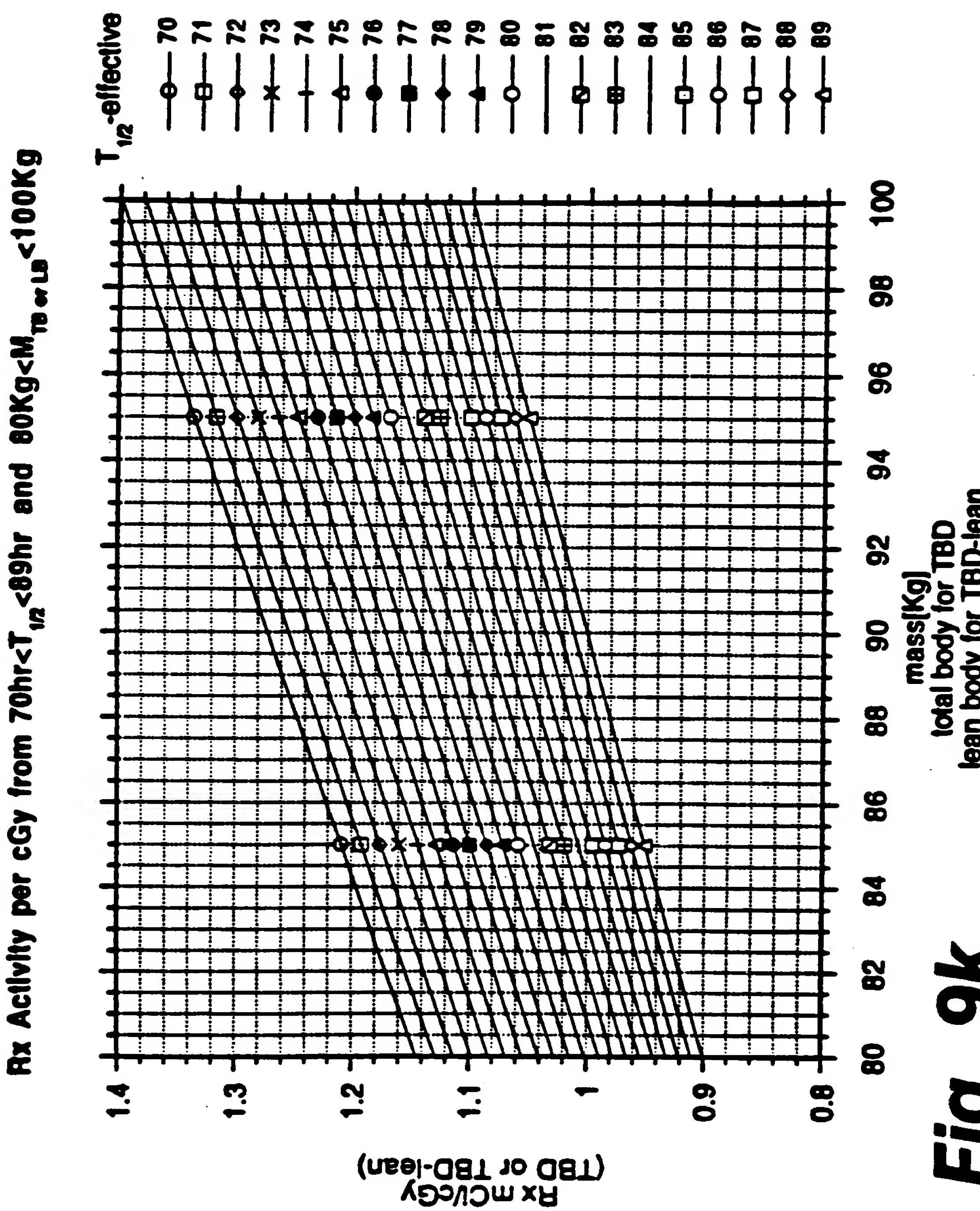

Rx Activity per cGy from 70hr<T1/2<89hr and 80Kg<M TB or LB<100Kg
T1/2-effective
70
71
72
73
74
75
76
77
78
79
80
81
82
83
84
85
86
87
88
89
Rx mCi/cGy
(TBD or TBD-lean)
1.4
1.3
1.2
1.1
1
0.9
0.8
80
82
84
86
88
90
92
94
96
98
100
mass[Kg]
total body for TBD
lean body for TBD-lean

Fig. 9k

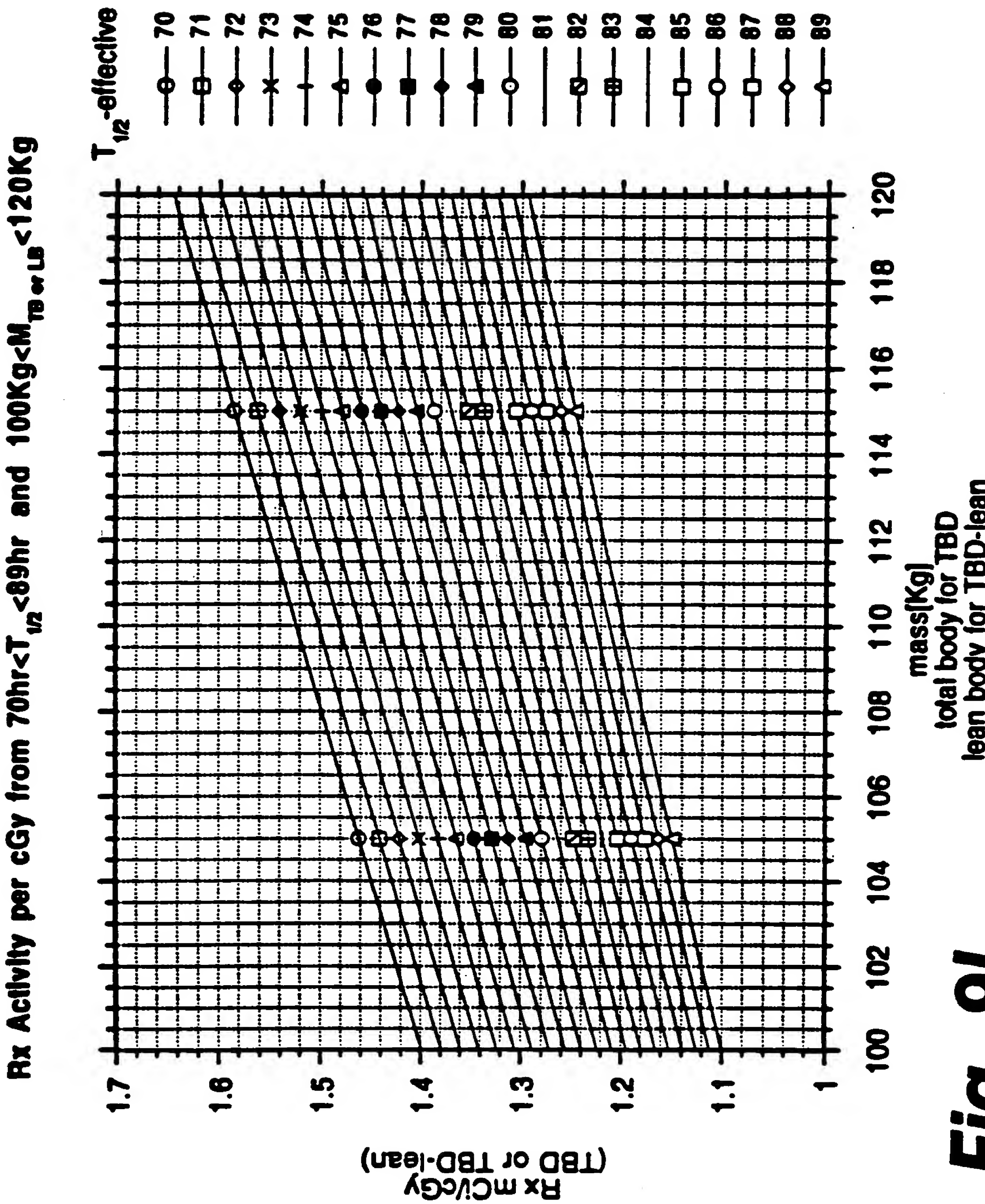

Rx Activity per cGy from 70hr<$T_{1/2}$<89hr and 100Kg<$M_{TB\ or\ LB}$<120Kg
$T_{1/2}$-effective
70
71
72
73
74
75
76
77
78
79
80
81
82
83
84
85
86
87
88
89
Rx mCi/cGy
(TBD or TBD-lean)
1.7
1.6
1.5
1.4
1.3
1.2
1.1
1
100
102
104
106
108
110
112
114
116
118
120
mass[Kg]
total body for TBD
lean body for TBD-lean

Fig. 9I

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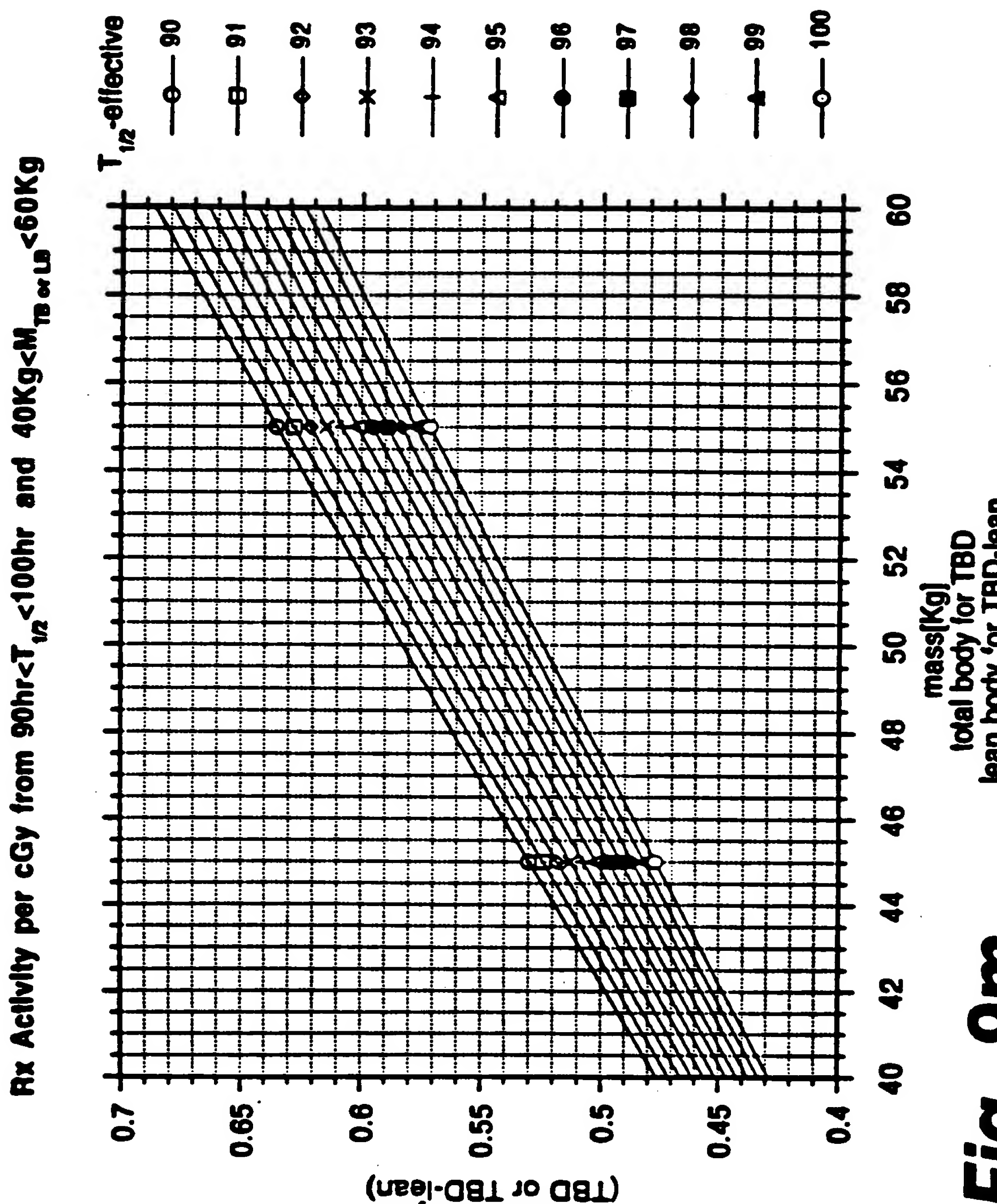

Rx Activity per cGy from 90hr<T1/2<100hr and 40Kg<M TB or LB<60Kg
T1/2-effective
90
91
92
93
94
95
96
97
98
99
100
Rx mCi/cGy
(TBD or TBD-lean)
0.7
0.65
0.6
0.55
0.5
0.45
0.4
40
42
44
46
48
50
52
54
56
58
60
mass[Kg]
total body for TBD
lean body for TBD-lean

Fig. 9m

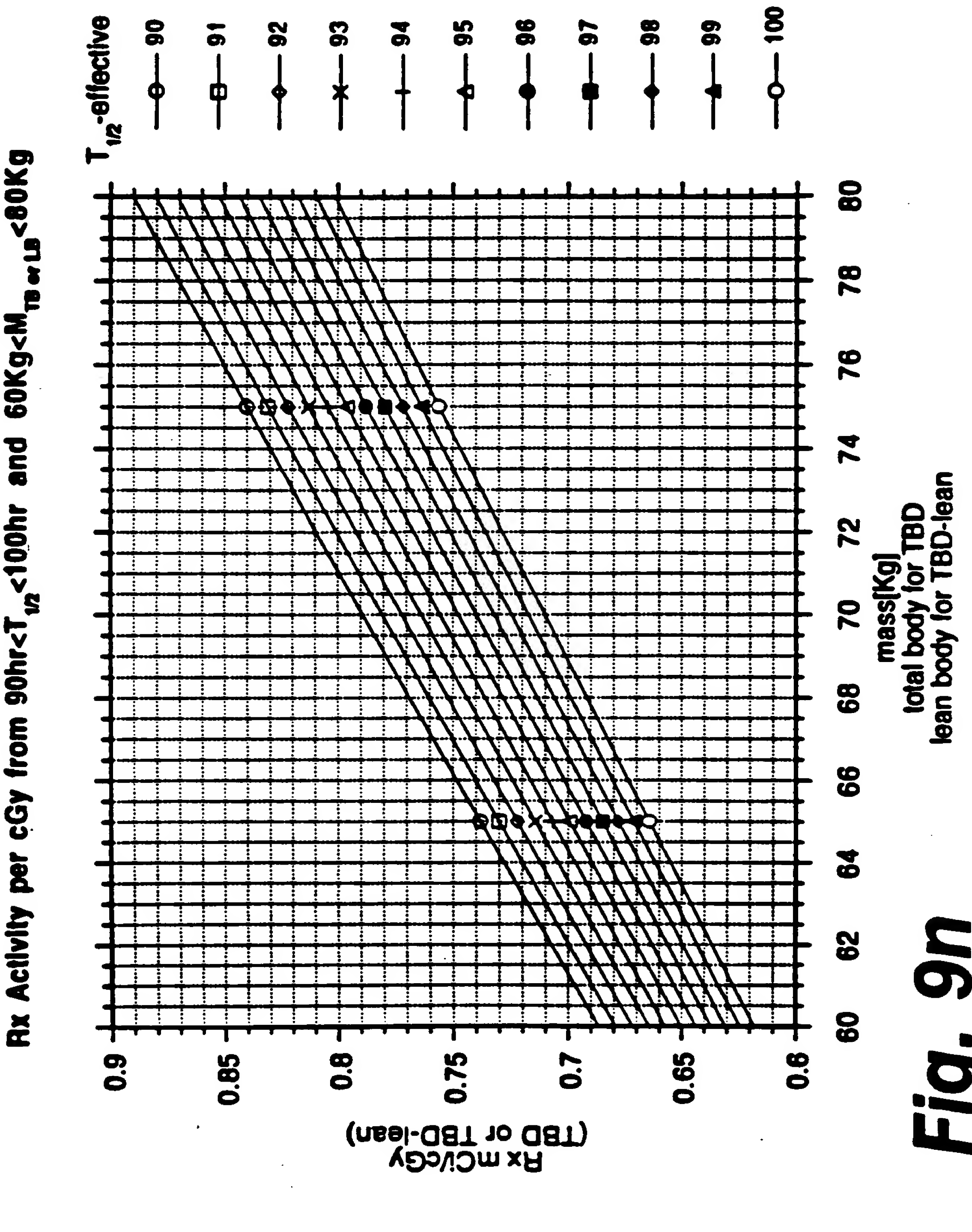
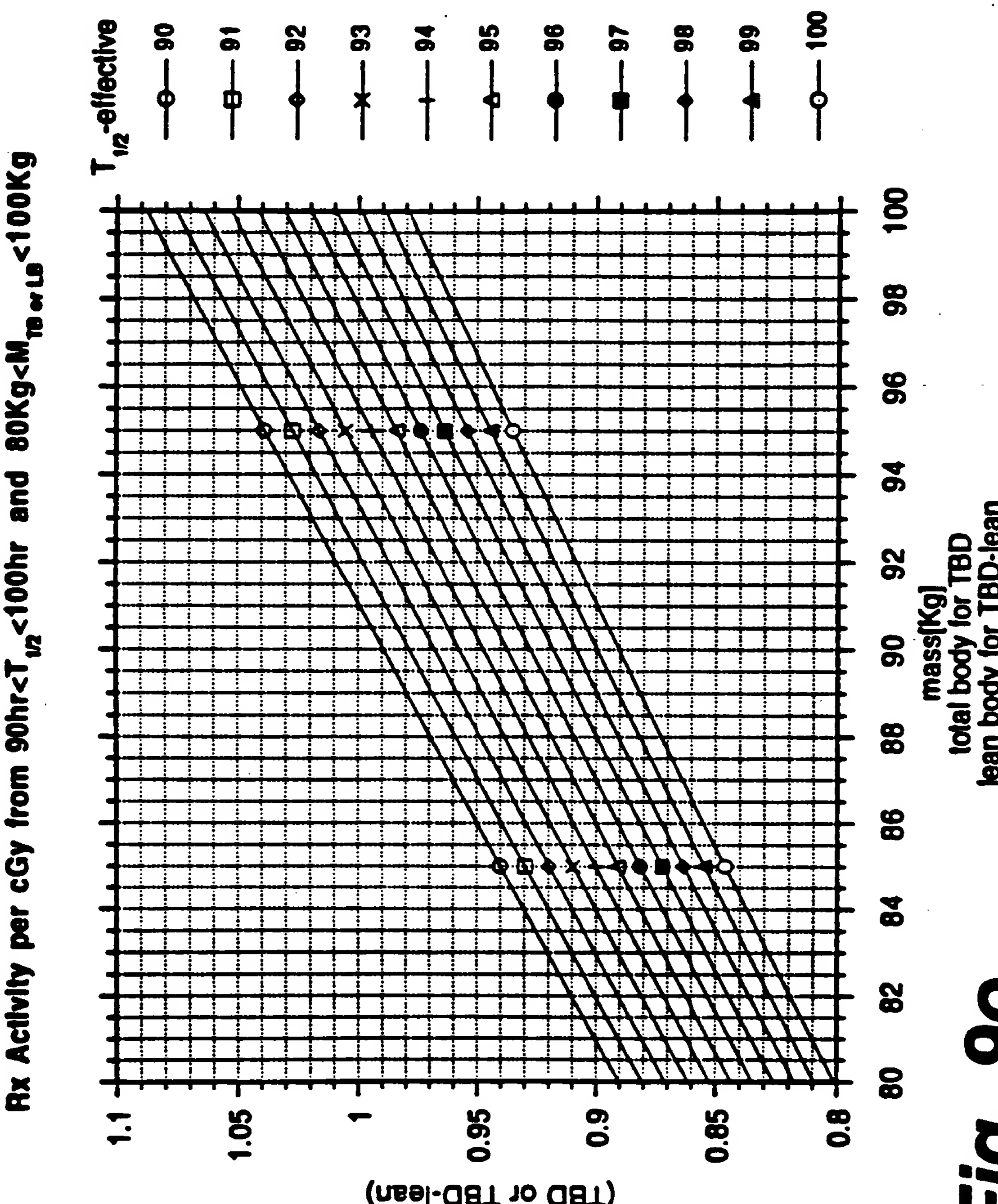

Rx Activity per cGy from 90hr<$T_{1/2}$<100hr and 60Kg<$M_{TB\ or\ LB}$<80Kg
$T_{1/2}$-effective
90
91
92
93
94
95
96
97
98
99
100
Rx mCi/cGy
(TBD or TBD-lean)
0.9
0.85
0.8
0.75
0.7
0.65
0.6
60
62
64
66
68
70
72
74
76
78
80
mass[Kg]
total body for TBD
lean body for TBD-lean

Fig. 9n



Rx Activity per cGy from 90hr<T1/2<100hr and 80Kg<M TB or LB<100Kg
T1/2-effective
90
91
92
93
94
95
96
97
98
99
100
Rx mCi/cGy
(TBD or TBD-lean)
1.1
1.05
1
0.95
0.9
0.85
0.8
80
82
84
86
88
90
92
94
96
98
100
mass[Kg]
total body for TBD
lean body for TBD-lean

Fig. 9o

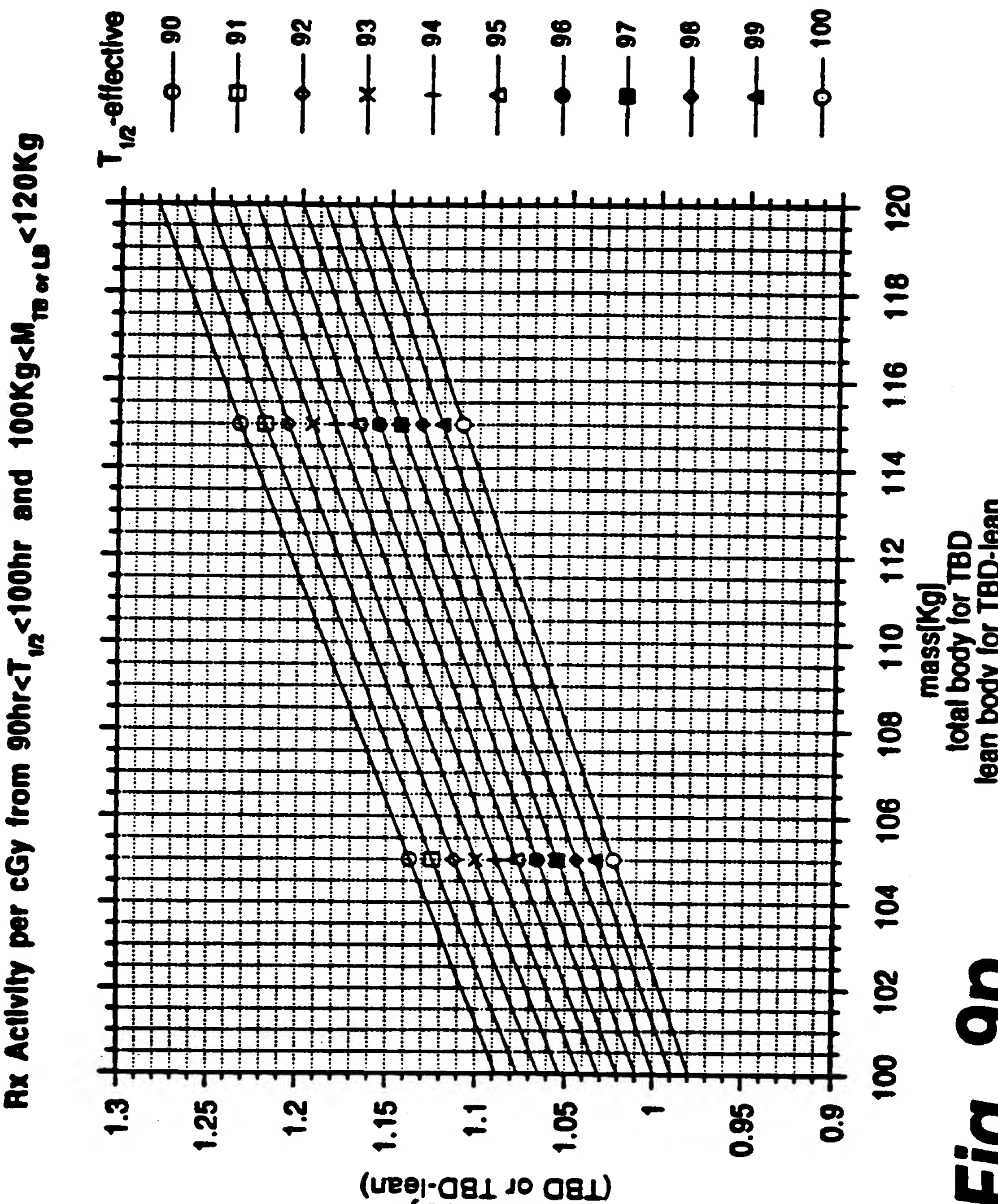

Rx Activity per cGy from 90hr<T1/2<100hr and 100Kg<MTB or LB<120Kg
T1/2-effective
90
91
92
93
94
95
96
97
98
99
100
Rx mCi/cGy
(TBD or TBD-lean)
1.3
1.25
1.2
1.15
1.1
1.05
1
0.95
0.9
100
102
104
106
108
110
112
114
116
118
120
mass[Kg]
total body for TBD
lean body for TBD-lean

Fig. 9p

Fig. 10a

mCi per cGy matrix

Activity per unit Total Body Dose (TBD) or Lean Body Dose (TBD-Lean) as a function of Total Body or Lean body mass and T1/2-effective

LBM estimates from:
Female: LBM = 45.5 + 0.91*(HT - 152) [HT in cm, LBM in Kg]
Male: LBM = 48.0 + 1.06*(HT - 152)

Total Body mass for Total Body dose
Lean Body mass(LBM) for Total Body Dose-Lean
|
V T-1/2[hr]-effective --> A0 [mCi/cGy]

mass[Kg]	30	31	32	33	34	35	36	37	38	39	40	41	42	43	44	45	46	47	48	49	50
40	1.429	1.383	1.339	1.299	1.261	1.226	1.191	1.158	1.128	1.099	1.071	1.045	1.020	0.997	0.974	0.952	0.932	0.912	0.893	0.875	0.857
41	1.461	1.414	1.370	1.328	1.289	1.252	1.217	1.185	1.153	1.124	1.096	1.069	1.044	1.019	0.996	0.974	0.953	0.933	0.913	0.894	0.877
42	1.493	1.445	1.400	1.357	1.317	1.280	1.244	1.211	1.178	1.148	1.120	1.093	1.068	1.042	1.019	0.995	0.974	0.953	0.933	0.914	0.896
43	1.525	1.476	1.430	1.387	1.346	1.307	1.271	1.237	1.204	1.173	1.144	1.116	1.090	1.064	1.040	1.017	0.995	0.974	0.953	0.934	0.915
44	1.557	1.507	1.460	1.416	1.374	1.335	1.298	1.263	1.229	1.198	1.168	1.139	1.112	1.086	1.062	1.038	1.016	0.994	0.973	0.953	0.934
45	1.588	1.538	1.490	1.445	1.402	1.362	1.324	1.289	1.255	1.222	1.192	1.163	1.135	1.109	1.083	1.059	1.036	1.014	0.993	0.973	0.953
46	1.621	1.569	1.520	1.474	1.430	1.389	1.351	1.314	1.280	1.247	1.216	1.186	1.158	1.131	1.105	1.081	1.057	1.035	1.013	0.992	0.973
47	1.653	1.599	1.549	1.502	1.458	1.417	1.377	1.340	1.305	1.271	1.239	1.209	1.180	1.153	1.127	1.102	1.078	1.055	1.033	1.012	0.992
48	1.684	1.630	1.579	1.531	1.486	1.444	1.404	1.366	1.330	1.296	1.263	1.232	1.203	1.175	1.148	1.123	1.098	1.075	1.053	1.031	1.011
49	1.716	1.661	1.609	1.560	1.514	1.471	1.430	1.391	1.355	1.320	1.287	1.256	1.226	1.197	1.170	1.144	1.119	1.095	1.072	1.051	1.030
50	1.747	1.691	1.638	1.588	1.542	1.498	1.456	1.417	1.380	1.344	1.311	1.279	1.248	1.219	1.191	1.165	1.140	1.115	1.092	1.070	1.049
51	1.778	1.722	1.668	1.617	1.570	1.525	1.482	1.442	1.404	1.368	1.334	1.302	1.271	1.241	1.213	1.186	1.160	1.136	1.112	1.089	1.067
52	1.810	1.752	1.697	1.646	1.597	1.552	1.509	1.468	1.429	1.393	1.358	1.325	1.293	1.263	1.234	1.207	1.181	1.156	1.132	1.109	1.086
53	1.842	1.782	1.727	1.674	1.625	1.578	1.535	1.493	1.454	1.417	1.381	1.348	1.316	1.285	1.256	1.228	1.201	1.176	1.151	1.128	1.105
54	1.873	1.813	1.756	1.703	1.653	1.605	1.561	1.518	1.479	1.441	1.405	1.371	1.338	1.307	1.277	1.249	1.222	1.196	1.171	1.147	1.124
55	1.904	1.843	1.785	1.731	1.680	1.632	1.587	1.544	1.503	1.465	1.428	1.393	1.360	1.329	1.298	1.270	1.242	1.216	1.190	1.166	1.143
56	1.936	1.873	1.815	1.760	1.708	1.658	1.613	1.569	1.528	1.489	1.452	1.416	1.383	1.350	1.320	1.290	1.262	1.235	1.210	1.185	1.161
57	1.967	1.903	1.844	1.788	1.735	1.685	1.639	1.595	1.553	1.513	1.475	1.439	1.405	1.372	1.341	1.311	1.283	1.255	1.229	1.204	1.180
58	1.998	1.933	1.873	1.816	1.763	1.712	1.665	1.620	1.577	1.537	1.498	1.462	1.427	1.394	1.362	1.332	1.303	1.275	1.249	1.223	1.199
59	2.029	1.963	1.902	1.844	1.790	1.738	1.691	1.645	1.602	1.561	1.522	1.485	1.449	1.416	1.383	1.353	1.323	1.295	1.269	1.242	1.217
60	2.060	1.993	1.931	1.873	1.818	1.765	1.717	1.670	1.626	1.585	1.545	1.507	1.471	1.437	1.404	1.373	1.343	1.315	1.287	1.261	1.236
61	2.091	2.023	1.960	1.901	1.845	1.792	1.742	1.695	1.651	1.608	1.568	1.530	1.493	1.459	1.426	1.394	1.364	1.335	1.307	1.280	1.254
62	2.122	2.053	1.989	1.929	1.872	1.818	1.768	1.720	1.675	1.632	1.591	1.552	1.515	1.480	1.447	1.414	1.384	1.354	1.326	1.299	1.273
63	2.152	2.083	2.018	1.957	1.899	1.845	1.794	1.745	1.699	1.656	1.614	1.575	1.537	1.502	1.468	1.435	1.404	1.374	1.345	1.318	1.291
64	2.183	2.113	2.047	1.985	1.926	1.871	1.819	1.770	1.724	1.679	1.637	1.597	1.559	1.523	1.488	1.455	1.424	1.394	1.364	1.337	1.310
65	2.214	2.143	2.076	2.013	1.953	1.898	1.845	1.795	1.748	1.703	1.660	1.620	1.581	1.545	1.509	1.476	1.444	1.413	1.384	1.355	1.328
66	2.245	2.172	2.104	2.040	1.980	1.924	1.870	1.820	1.772	1.727	1.683	1.642	1.603	1.566	1.530	1.496	1.464	1.433	1.403	1.374	1.347
67	2.275	2.202	2.133	2.068	2.006	1.950	1.896	1.845	1.796	1.750	1.706	1.665	1.625	1.587	1.551	1.517	1.484	1.452	1.422	1.393	1.365
68	2.306	2.231	2.162	2.096	2.033	1.976	1.922	1.870	1.820	1.774	1.729	1.687	1.647	1.609	1.572	1.537	1.504	1.472	1.441	1.412	1.383
69	2.336	2.261	2.190	2.124	2.062	2.003	1.947	1.894	1.845	1.797	1.752	1.710	1.669	1.630	1.593	1.558	1.524	1.491	1.460	1.430	1.402
70	2.367	2.291	2.219	2.152	2.088	2.029	1.972	1.919	1.869	1.821	1.775	1.732	1.691	1.651	1.614	1.578	1.544	1.511	1.479	1.449	1.420
71	2.398	2.320	2.248	2.180	2.115	2.055	1.998	1.944	1.893	1.844	1.798	1.754	1.713	1.673	1.635	1.598	1.564	1.530	1.498	1.468	1.439
72	2.428	2.350	2.276	2.207	2.142	2.081	2.023	1.969	1.917	1.868	1.821	1.777	1.734	1.694	1.656	1.618	1.584	1.550	1.518	1.487	1.457
73	2.459	2.379	2.305	2.235	2.169	2.107	2.049	1.993	1.941	1.891	1.844	1.799	1.756	1.715	1.676	1.639	1.603	1.569	1.537	1.505	1.475
74	2.489	2.409	2.333	2.263	2.196	2.133	2.074	2.018	1.965	1.915	1.867	1.821	1.778	1.737	1.697	1.659	1.623	1.589	1.556	1.524	1.493
75	2.520	2.438	2.362	2.290	2.223	2.159	2.100	2.043	1.989	1.938	1.890	1.844	1.800	1.758	1.718	1.680	1.643	1.608	1.575	1.543	1.512
76	2.550	2.468	2.391	2.318	2.250	2.186	2.125	2.067	2.013	1.961	1.912	1.866	1.821	1.779	1.739	1.700	1.663	1.628	1.594	1.561	1.530
77	2.580	2.497	2.419	2.346	2.277	2.212	2.150	2.092	2.037	1.985	1.935	1.888	1.843	1.800	1.759	1.720	1.683	1.647	1.613	1.580	1.548
78	2.610	2.526	2.447	2.373	2.303	2.238	2.175	2.117	2.061	2.008	1.958	1.910	1.865	1.821	1.780	1.740	1.702	1.666	1.632	1.598	1.566
79	2.641	2.555	2.476	2.401	2.330	2.263	2.201	2.141	2.085	2.031	1.980	1.932	1.886	1.842	1.800	1.760	1.722	1.686	1.650	1.617	1.584
80	2.671	2.585	2.504	2.428	2.357	2.289	2.226	2.165	2.108	2.054	2.003	1.954	1.908	1.863	1.821	1.780	1.742	1.705	1.669	1.635	1.602
81	2.701	2.614	2.532	2.455	2.383	2.315	2.251	2.190	2.132	2.077	2.025	1.976	1.929	1.884	1.841	1.800	1.761	1.724	1.688	1.653	1.620
82	2.731	2.642	2.560	2.482	2.409	2.340	2.276	2.214	2.156	2.100	2.048	1.998	1.950	1.905	1.862	1.820	1.781	1.743	1.707	1.672	1.638
83	2.760	2.671	2.588	2.509	2.436	2.366	2.300	2.238	2.179	2.123	2.070	2.020	1.972	1.926	1.882	1.840	1.800	1.762	1.725	1.690	1.656

Fig. 10b

mCi per cGy matrix

Total Bod
Lean Bod
|
V

T-1/2[hr]-effective --> A0 [mCi/cGy]

mass[Kg]	51	52	53	54	55	56	57	58	59	60	61	62	63	64	65	66	67	68	69	70	71
40	0.840	0.824	0.809	0.794	0.779	0.765	0.752	0.739	0.726	0.714	0.703	0.691	0.680	0.670	0.659	0.649	0.640	0.630	0.621	0.612	0.604
41	0.859	0.843	0.827	0.812	0.797	0.783	0.769	0.756	0.743	0.730	0.719	0.707	0.696	0.685	0.674	0.664	0.654	0.645	0.635	0.626	0.617
42	0.878	0.861	0.845	0.829	0.814	0.800	0.786	0.772	0.759	0.747	0.734	0.722	0.711	0.700	0.689	0.678	0.668	0.659	0.649	0.640	0.631
43	0.897	0.880	0.863	0.847	0.832	0.817	0.803	0.789	0.776	0.763	0.750	0.738	0.726	0.715	0.704	0.693	0.683	0.673	0.663	0.654	0.644
44	0.916	0.898	0.881	0.865	0.849	0.834	0.820	0.805	0.792	0.779	0.766	0.753	0.741	0.730	0.718	0.708	0.697	0.687	0.677	0.667	0.658
45	0.936	0.917	0.899	0.883	0.867	0.851	0.836	0.822	0.808	0.795	0.782	0.769	0.757	0.745	0.733	0.722	0.712	0.701	0.691	0.681	0.671
46	0.953	0.935	0.917	0.900	0.884	0.868	0.853	0.839	0.824	0.810	0.797	0.784	0.772	0.760	0.748	0.737	0.726	0.715	0.705	0.695	0.685
47	0.972	0.953	0.935	0.918	0.901	0.885	0.870	0.855	0.840	0.826	0.813	0.800	0.787	0.775	0.763	0.751	0.740	0.729	0.719	0.709	0.698
48	0.991	0.972	0.953	0.936	0.919	0.902	0.886	0.871	0.856	0.842	0.828	0.815	0.802	0.790	0.777	0.766	0.754	0.743	0.732	0.722	0.712
49	1.009	0.990	0.971	0.953	0.936	0.919	0.903	0.888	0.873	0.858	0.844	0.830	0.817	0.804	0.792	0.780	0.768	0.757	0.746	0.735	0.725
50	1.028	1.008	0.989	0.971	0.953	0.936	0.920	0.904	0.889	0.874	0.859	0.846	0.832	0.819	0.807	0.794	0.782	0.771	0.760	0.749	0.738
51	1.046	1.026	1.007	0.988	0.970	0.953	0.936	0.920	0.905	0.889	0.875	0.861	0.847	0.834	0.821	0.809	0.797	0.785	0.773	0.762	0.752
52	1.065	1.044	1.025	1.006	0.987	0.970	0.953	0.936	0.921	0.905	0.890	0.876	0.862	0.849	0.836	0.823	0.811	0.799	0.787	0.776	0.765
53	1.083	1.063	1.043	1.023	1.005	0.987	0.969	0.953	0.937	0.921	0.906	0.891	0.877	0.863	0.850	0.837	0.825	0.813	0.801	0.789	0.778
54	1.102	1.081	1.060	1.041	1.022	1.003	0.986	0.969	0.952	0.937	0.921	0.906	0.892	0.878	0.864	0.851	0.838	0.826	0.814	0.803	0.791
55	1.120	1.099	1.078	1.058	1.039	1.020	1.002	0.985	0.968	0.952	0.937	0.921	0.907	0.893	0.879	0.866	0.853	0.840	0.828	0.816	0.805
56	1.139	1.117	1.096	1.076	1.056	1.037	1.019	1.001	0.984	0.968	0.952	0.937	0.922	0.907	0.893	0.880	0.867	0.854	0.842	0.830	0.818
57	1.157	1.135	1.113	1.093	1.073	1.054	1.035	1.017	1.000	0.983	0.967	0.952	0.937	0.922	0.908	0.894	0.881	0.868	0.855	0.843	0.831
58	1.176	1.153	1.131	1.110	1.090	1.070	1.052	1.033	1.016	0.999	0.983	0.967	0.951	0.936	0.922	0.908	0.895	0.881	0.869	0.856	0.844
59	1.193	1.171	1.148	1.127	1.107	1.087	1.068	1.049	1.032	1.014	0.998	0.982	0.966	0.951	0.936	0.922	0.908	0.895	0.882	0.870	0.857
60	1.212	1.189	1.166	1.144	1.124	1.104	1.084	1.065	1.047	1.030	1.013	0.997	0.981	0.966	0.951	0.936	0.922	0.908	0.896	0.883	0.870
61	1.230	1.206	1.183	1.162	1.140	1.120	1.100	1.081	1.063	1.045	1.028	1.012	0.996	0.980	0.965	0.950	0.936	0.922	0.909	0.896	0.883
62	1.248	1.224	1.201	1.179	1.157	1.137	1.117	1.097	1.079	1.061	1.043	1.027	1.010	0.995	0.979	0.964	0.950	0.936	0.922	0.909	0.896
63	1.266	1.242	1.219	1.196	1.174	1.153	1.133	1.113	1.094	1.076	1.058	1.042	1.025	1.009	0.993	0.978	0.964	0.950	0.936	0.922	0.909
64	1.284	1.260	1.236	1.213	1.191	1.170	1.149	1.129	1.110	1.092	1.074	1.056	1.040	1.023	1.008	0.992	0.978	0.963	0.949	0.936	0.922
65	1.302	1.277	1.253	1.230	1.208	1.186	1.165	1.145	1.126	1.107	1.089	1.071	1.054	1.038	1.022	1.006	0.991	0.977	0.963	0.949	0.935
66	1.320	1.295	1.270	1.247	1.224	1.202	1.181	1.161	1.141	1.122	1.104	1.086	1.069	1.052	1.036	1.020	1.005	0.990	0.976	0.962	0.948
67	1.339	1.313	1.288	1.264	1.241	1.219	1.197	1.177	1.157	1.138	1.119	1.101	1.083	1.067	1.050	1.034	1.019	1.004	0.989	0.975	0.961
68	1.356	1.330	1.305	1.281	1.258	1.235	1.214	1.193	1.172	1.153	1.134	1.116	1.098	1.081	1.064	1.048	1.032	1.017	1.003	0.988	0.974
69	1.374	1.348	1.323	1.298	1.274	1.252	1.230	1.209	1.188	1.169	1.149	1.131	1.113	1.095	1.078	1.062	1.046	1.031	1.016	1.001	0.987
70	1.392	1.366	1.340	1.315	1.291	1.268	1.246	1.224	1.204	1.183	1.164	1.145	1.127	1.110	1.092	1.076	1.060	1.044	1.029	1.014	1.000
71	1.410	1.383	1.357	1.332	1.308	1.284	1.262	1.240	1.219	1.199	1.179	1.160	1.142	1.124	1.107	1.090	1.074	1.058	1.042	1.028	1.013
72	1.428	1.401	1.374	1.348	1.324	1.301	1.278	1.256	1.235	1.214	1.194	1.175	1.156	1.138	1.121	1.104	1.087	1.071	1.056	1.041	1.026
73	1.446	1.418	1.392	1.366	1.341	1.317	1.294	1.272	1.250	1.229	1.209	1.190	1.171	1.152	1.135	1.118	1.101	1.085	1.069	1.054	1.039
74	1.464	1.436	1.409	1.383	1.358	1.333	1.310	1.287	1.266	1.245	1.224	1.204	1.185	1.167	1.149	1.131	1.115	1.098	1.082	1.067	1.052
75	1.482	1.454	1.426	1.400	1.374	1.350	1.326	1.303	1.281	1.260	1.239	1.219	1.200	1.181	1.163	1.145	1.128	1.112	1.096	1.080	1.065
76	1.500	1.471	1.443	1.417	1.391	1.366	1.342	1.319	1.297	1.275	1.254	1.234	1.214	1.195	1.177	1.159	1.142	1.125	1.109	1.093	1.077
77	1.518	1.489	1.460	1.433	1.407	1.382	1.358	1.335	1.312	1.290	1.269	1.248	1.228	1.209	1.191	1.173	1.156	1.139	1.122	1.106	1.090
78	1.536	1.506	1.478	1.450	1.424	1.398	1.374	1.350	1.327	1.305	1.284	1.263	1.243	1.224	1.205	1.187	1.169	1.152	1.135	1.119	1.103
79	1.553	1.523	1.495	1.467	1.440	1.415	1.390	1.366	1.343	1.320	1.299	1.278	1.257	1.238	1.219	1.200	1.182	1.165	1.148	1.132	1.116
80	1.571	1.541	1.512	1.484	1.457	1.431	1.406	1.381	1.358	1.335	1.313	1.292	1.272	1.252	1.233	1.214	1.196	1.178	1.161	1.145	1.128
81	1.589	1.558	1.529	1.500	1.473	1.447	1.421	1.397	1.373	1.350	1.328	1.307	1.286	1.266	1.246	1.228	1.209	1.191	1.174	1.157	1.141
82	1.606	1.575	1.546	1.517	1.489	1.463	1.437	1.412	1.389	1.366	1.343	1.321	1.300	1.280	1.260	1.241	1.223	1.205	1.187	1.170	1.154
83	1.624	1.592	1.562	1.534	1.506	1.479	1.453	1.428	1.404	1.380	1.358	1.336	1.314	1.294	1.274	1.255	1.236	1.218	1.200	1.183	1.166

Fig. 10c

mCi per cGy matrix

Total Bod
Lean Bod
|
V

T-1/2[hr]-effective -->   A0 [mCi/cGy]

mass[Kg]	72	73	74	75	76	77	78	79	80	81	82	83	84	85	86	87	88	89	90	91	92
40	0.595	0.587	0.579	0.571	0.564	0.557	0.549	0.543	0.536	0.529	0.523	0.516	0.510	0.504	0.498	0.493	0.487	0.482	0.476	0.471	0.466
41	0.609	0.600	0.592	0.584	0.577	0.569	0.562	0.555	0.548	0.541	0.534	0.528	0.522	0.516	0.510	0.504	0.498	0.492	0.487	0.482	0.476
42	0.622	0.614	0.605	0.597	0.589	0.582	0.574	0.567	0.560	0.553	0.546	0.540	0.533	0.527	0.521	0.515	0.509	0.503	0.498	0.492	0.487
43	0.636	0.627	0.618	0.610	0.602	0.594	0.587	0.579	0.572	0.565	0.558	0.551	0.545	0.538	0.532	0.526	0.520	0.514	0.508	0.503	0.497
44	0.649	0.640	0.631	0.623	0.615	0.607	0.599	0.591	0.584	0.577	0.570	0.563	0.556	0.550	0.543	0.537	0.531	0.525	0.519	0.513	0.508
45	0.662	0.653	0.644	0.636	0.627	0.619	0.611	0.603	0.596	0.588	0.581	0.574	0.568	0.561	0.554	0.548	0.542	0.536	0.530	0.524	0.518
46	0.675	0.666	0.657	0.648	0.640	0.632	0.623	0.616	0.608	0.600	0.593	0.586	0.579	0.572	0.566	0.559	0.553	0.546	0.540	0.534	0.529
47	0.689	0.679	0.670	0.661	0.652	0.644	0.636	0.628	0.620	0.612	0.605	0.597	0.590	0.583	0.577	0.570	0.563	0.557	0.551	0.545	0.539
48	0.702	0.692	0.683	0.674	0.665	0.656	0.648	0.640	0.632	0.624	0.616	0.609	0.602	0.594	0.588	0.581	0.574	0.568	0.561	0.555	0.549
49	0.715	0.705	0.696	0.686	0.677	0.668	0.660	0.652	0.643	0.636	0.628	0.620	0.613	0.606	0.599	0.592	0.585	0.578	0.572	0.566	0.560
50	0.728	0.718	0.708	0.699	0.690	0.681	0.672	0.664	0.655	0.647	0.639	0.632	0.624	0.617	0.610	0.603	0.596	0.589	0.582	0.576	0.570
51	0.741	0.731	0.721	0.712	0.702	0.693	0.684	0.676	0.667	0.659	0.651	0.643	0.635	0.628	0.621	0.613	0.606	0.600	0.593	0.586	0.580
52	0.754	0.744	0.734	0.724	0.716	0.705	0.696	0.687	0.679	0.671	0.662	0.654	0.647	0.639	0.632	0.624	0.617	0.610	0.603	0.597	0.590
53	0.767	0.757	0.747	0.737	0.727	0.718	0.708	0.699	0.691	0.682	0.674	0.666	0.658	0.650	0.642	0.635	0.628	0.621	0.614	0.607	0.601
54	0.780	0.770	0.759	0.749	0.739	0.730	0.720	0.711	0.702	0.694	0.686	0.677	0.669	0.661	0.653	0.646	0.638	0.631	0.624	0.618	0.611
55	0.794	0.783	0.772	0.762	0.752	0.742	0.732	0.723	0.714	0.705	0.697	0.688	0.680	0.672	0.664	0.657	0.649	0.642	0.635	0.628	0.621
56	0.807	0.795	0.785	0.774	0.764	0.754	0.744	0.736	0.726	0.717	0.708	0.700	0.691	0.683	0.675	0.667	0.660	0.652	0.645	0.638	0.631
57	0.819	0.808	0.797	0.787	0.776	0.766	0.756	0.747	0.738	0.728	0.720	0.711	0.702	0.694	0.686	0.678	0.670	0.663	0.656	0.648	0.641
58	0.832	0.821	0.810	0.799	0.789	0.778	0.768	0.759	0.749	0.740	0.731	0.722	0.714	0.705	0.697	0.689	0.681	0.673	0.666	0.659	0.651
59	0.846	0.834	0.823	0.812	0.801	0.790	0.780	0.770	0.761	0.751	0.742	0.733	0.726	0.716	0.708	0.700	0.692	0.684	0.676	0.669	0.662
60	0.858	0.847	0.835	0.824	0.813	0.803	0.792	0.782	0.772	0.763	0.754	0.745	0.736	0.727	0.719	0.710	0.702	0.694	0.687	0.679	0.672
61	0.871	0.859	0.848	0.836	0.825	0.815	0.804	0.794	0.784	0.774	0.765	0.756	0.747	0.738	0.729	0.721	0.713	0.705	0.697	0.689	0.682
62	0.884	0.872	0.860	0.849	0.837	0.827	0.816	0.806	0.796	0.786	0.776	0.767	0.758	0.749	0.740	0.732	0.723	0.715	0.707	0.699	0.692
63	0.897	0.885	0.873	0.861	0.850	0.839	0.828	0.817	0.807	0.797	0.787	0.778	0.769	0.760	0.751	0.742	0.734	0.726	0.717	0.710	0.702
64	0.910	0.897	0.885	0.873	0.862	0.851	0.840	0.829	0.819	0.809	0.799	0.789	0.780	0.771	0.762	0.753	0.744	0.736	0.728	0.720	0.712
65	0.922	0.910	0.898	0.886	0.874	0.863	0.852	0.841	0.830	0.820	0.810	0.800	0.791	0.781	0.772	0.763	0.755	0.746	0.738	0.730	0.722
66	0.935	0.922	0.910	0.898	0.886	0.874	0.863	0.852	0.842	0.831	0.821	0.811	0.802	0.792	0.783	0.774	0.765	0.757	0.748	0.740	0.732
67	0.948	0.935	0.922	0.910	0.898	0.886	0.875	0.864	0.853	0.843	0.832	0.822	0.813	0.803	0.794	0.785	0.776	0.767	0.758	0.750	0.742
68	0.961	0.948	0.935	0.922	0.910	0.898	0.887	0.876	0.865	0.854	0.844	0.833	0.824	0.814	0.804	0.795	0.786	0.777	0.769	0.760	0.752
69	0.974	0.960	0.947	0.935	0.922	0.910	0.899	0.887	0.876	0.865	0.855	0.844	0.834	0.825	0.815	0.806	0.797	0.788	0.779	0.770	0.762
70	0.986	0.973	0.960	0.947	0.934	0.922	0.910	0.899	0.888	0.877	0.866	0.856	0.845	0.835	0.826	0.816	0.807	0.798	0.789	0.780	0.772
71	0.999	0.985	0.972	0.959	0.946	0.934	0.922	0.910	0.899	0.888	0.877	0.867	0.856	0.846	0.837	0.827	0.817	0.808	0.799	0.790	0.782
72	1.012	0.998	0.984	0.971	0.959	0.946	0.934	0.922	0.911	0.899	0.888	0.878	0.867	0.857	0.847	0.837	0.828	0.819	0.809	0.800	0.792
73	1.024	1.010	0.997	0.983	0.971	0.958	0.946	0.934	0.922	0.911	0.899	0.889	0.878	0.868	0.858	0.848	0.838	0.829	0.820	0.811	0.802
74	1.037	1.023	1.009	0.996	0.983	0.970	0.957	0.945	0.933	0.922	0.911	0.900	0.889	0.878	0.868	0.858	0.848	0.839	0.830	0.821	0.812
75	1.050	1.036	1.021	1.008	0.995	0.982	0.969	0.957	0.945	0.933	0.922	0.911	0.900	0.889	0.879	0.869	0.859	0.849	0.840	0.831	0.822
76	1.062	1.048	1.034	1.020	1.007	0.993	0.981	0.968	0.956	0.944	0.933	0.922	0.911	0.900	0.890	0.879	0.869	0.860	0.850	0.841	0.831
77	1.076	1.060	1.046	1.032	1.019	1.005	0.992	0.980	0.968	0.956	0.944	0.933	0.922	0.911	0.900	0.890	0.880	0.870	0.860	0.851	0.841
78	1.088	1.073	1.058	1.044	1.030	1.017	1.004	0.991	0.979	0.967	0.955	0.944	0.932	0.921	0.911	0.900	0.890	0.880	0.870	0.861	0.851
79	1.100	1.085	1.071	1.056	1.042	1.029	1.016	1.003	0.990	0.978	0.966	0.954	0.943	0.932	0.921	0.911	0.900	0.890	0.880	0.871	0.861
80	1.113	1.098	1.083	1.068	1.054	1.041	1.027	1.014	1.002	0.989	0.977	0.965	0.954	0.943	0.932	0.921	0.910	0.900	0.890	0.880	0.871
81	1.126	1.110	1.095	1.080	1.066	1.052	1.039	1.026	1.013	1.000	0.988	0.976	0.965	0.953	0.942	0.931	0.921	0.910	0.900	0.890	0.881
82	1.138	1.122	1.107	1.092	1.078	1.064	1.050	1.037	1.024	1.011	0.999	0.987	0.975	0.964	0.953	0.942	0.931	0.920	0.910	0.900	0.890
83	1.150	1.134	1.119	1.104	1.089	1.075	1.062	1.048	1.035	1.022	1.010	0.998	0.986	0.974	0.963	0.952	0.941	0.930	0.920	0.910	0.900

Fig. 10d

mCi per cGy matrix

Total Bod
Lean Bod
|
V

mass[Kg]	T-1/2[hr]-effective --> 93	94	95	96	97	98	AO [mCi/cGy] 99	100
40	0.461	0.456	0.451	0.446	0.442	0.437	0.433	0.429
41	0.471	0.466	0.461	0.457	0.452	0.447	0.443	0.438
42	0.482	0.477	0.472	0.467	0.462	0.457	0.452	0.448
43	0.492	0.487	0.482	0.477	0.472	0.467	0.462	0.458
44	0.502	0.497	0.492	0.487	0.482	0.477	0.472	0.467
45	0.513	0.507	0.502	0.497	0.491	0.486	0.482	0.477
46	0.523	0.517	0.512	0.507	0.501	0.496	0.491	0.486
47	0.533	0.527	0.522	0.516	0.511	0.506	0.501	0.496
48	0.543	0.538	0.532	0.526	0.521	0.516	0.510	0.505
49	0.554	0.548	0.542	0.536	0.531	0.525	0.520	0.515
50	0.564	0.558	0.552	0.546	0.540	0.535	0.530	0.524
51	0.574	0.568	0.562	0.556	0.550	0.545	0.539	0.534
52	0.584	0.578	0.572	0.566	0.560	0.554	0.549	0.543
53	0.594	0.588	0.582	0.576	0.570	0.564	0.558	0.553
54	0.604	0.598	0.592	0.585	0.579	0.573	0.568	0.562
55	0.614	0.608	0.601	0.595	0.589	0.583	0.577	0.571
56	0.624	0.618	0.611	0.605	0.599	0.593	0.587	0.581
57	0.634	0.628	0.621	0.615	0.608	0.602	0.596	0.590
58	0.644	0.638	0.631	0.624	0.618	0.612	0.605	0.599
59	0.654	0.648	0.641	0.634	0.628	0.621	0.615	0.609
60	0.664	0.657	0.650	0.644	0.637	0.631	0.624	0.618
61	0.674	0.667	0.660	0.653	0.647	0.640	0.634	0.627
62	0.684	0.677	0.670	0.663	0.656	0.649	0.643	0.636
63	0.694	0.687	0.680	0.673	0.666	0.659	0.652	0.646
64	0.704	0.697	0.690	0.682	0.675	0.668	0.662	0.655
65	0.714	0.707	0.699	0.692	0.685	0.678	0.671	0.664
66	0.724	0.716	0.709	0.701	0.694	0.687	0.680	0.673
67	0.734	0.726	0.719	0.711	0.704	0.697	0.689	0.683
68	0.744	0.736	0.728	0.721	0.713	0.706	0.698	0.692
69	0.754	0.746	0.738	0.730	0.723	0.716	0.708	0.701
70	0.764	0.756	0.747	0.740	0.732	0.725	0.717	0.710
71	0.773	0.765	0.757	0.749	0.742	0.734	0.727	0.719
72	0.783	0.775	0.767	0.759	0.751	0.743	0.736	0.728
73	0.793	0.785	0.776	0.768	0.760	0.753	0.745	0.738
74	0.803	0.794	0.786	0.778	0.770	0.762	0.754	0.747
75	0.813	0.804	0.796	0.787	0.779	0.771	0.763	0.756
76	0.823	0.814	0.805	0.797	0.788	0.781	0.773	0.765
77	0.832	0.823	0.815	0.806	0.798	0.790	0.782	0.774
78	0.842	0.833	0.824	0.816	0.807	0.799	0.791	0.783
79	0.852	0.843	0.834	0.825	0.817	0.808	0.800	0.792
80	0.862	0.852	0.843	0.835	0.826	0.818	0.809	0.801
81	0.871	0.862	0.853	0.844	0.835	0.827	0.818	0.810
82	0.881	0.871	0.862	0.853	0.844	0.836	0.827	0.819
83	0.890	0.881	0.872	0.863	0.854	0.845	0.836	0.828

Fig. 10e

mCi per cGy matrix

Activity per unit Total Body Dose (TBD) or Lean Body Dose (TBD-Lean) as a function of Total Body or Lean body mass and T1/2-effective

LBM estimates from:

Total Body mass for Total Body dose — Female: LBM = 45.5 + 0.91*(HT - 152) [HT in cm, LBM in Kg]

Lean Body mass(LBM) for Total Body Dose-Lean — Male: LBM = 48.0 + 1.06*(HT - 152)

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V T-1/2[hr]-effective --> A0 [mCi/cGy]

mass[Kg]	30	31	32	33	34	35	36	37	38	39	40	41	42	43	44	45	46	47	48	49	50
84	2.790	2.700	2.618	2.536	2.462	2.391	2.325	2.262	2.203	2.146	2.093	2.041	1.993	1.947	1.902	1.860	1.820	1.781	1.744	1.708	1.674
85	2.820	2.729	2.643	2.563	2.489	2.417	2.350	2.286	2.226	2.169	2.115	2.063	2.014	1.967	1.923	1.880	1.839	1.800	1.762	1.726	1.692
86	2.848	2.757	2.671	2.590	2.514	2.442	2.374	2.310	2.249	2.192	2.137	2.085	2.035	1.988	1.943	1.900	1.858	1.819	1.781	1.744	1.710
87	2.876	2.786	2.699	2.617	2.540	2.468	2.399	2.334	2.273	2.215	2.159	2.107	2.056	2.009	1.963	1.919	1.878	1.838	1.799	1.763	1.727
88	2.906	2.815	2.727	2.644	2.566	2.493	2.424	2.358	2.296	2.237	2.181	2.128	2.077	2.029	1.983	1.939	1.897	1.856	1.818	1.781	1.745
89	2.938	2.843	2.754	2.671	2.592	2.518	2.448	2.382	2.320	2.260	2.204	2.150	2.099	2.050	2.003	1.959	1.916	1.875	1.836	1.799	1.763
90	2.968	2.872	2.782	2.698	2.618	2.544	2.473	2.406	2.343	2.283	2.226	2.171	2.120	2.070	2.023	1.979	1.935	1.894	1.855	1.817	1.781
91	2.997	2.901	2.810	2.725	2.645	2.569	2.498	2.430	2.366	2.306	2.248	2.193	2.141	2.091	2.044	1.998	1.955	1.913	1.873	1.835	1.798
92	3.027	2.929	2.838	2.752	2.671	2.595	2.522	2.454	2.390	2.328	2.270	2.215	2.162	2.112	2.064	2.018	1.974	1.932	1.892	1.853	1.816
93	3.057	2.958	2.866	2.779	2.697	2.620	2.547	2.478	2.413	2.351	2.293	2.237	2.183	2.133	2.084	2.038	1.993	1.951	1.910	1.871	1.834
94	3.086	2.987	2.893	2.806	2.723	2.645	2.572	2.502	2.437	2.374	2.315	2.258	2.205	2.153	2.104	2.058	2.013	1.970	1.929	1.890	1.852
95	3.116	3.016	2.921	2.833	2.749	2.671	2.597	2.527	2.460	2.397	2.337	2.280	2.226	2.174	2.125	2.077	2.032	1.989	1.948	1.908	1.870
96	3.146	3.044	2.949	2.860	2.776	2.696	2.621	2.551	2.483	2.420	2.359	2.302	2.247	2.195	2.145	2.097	2.052	2.008	1.966	1.926	1.887
97	3.175	3.073	2.977	2.887	2.802	2.722	2.646	2.575	2.507	2.443	2.381	2.323	2.268	2.215	2.165	2.117	2.071	2.027	1.985	1.944	1.905
98	3.205	3.101	3.005	2.914	2.828	2.747	2.671	2.598	2.530	2.465	2.404	2.345	2.289	2.236	2.185	2.137	2.090	2.046	2.003	1.962	1.923
99	3.234	3.130	3.032	2.940	2.854	2.772	2.695	2.622	2.553	2.488	2.426	2.367	2.310	2.257	2.205	2.156	2.109	2.064	2.021	1.980	1.941
100	3.264	3.158	3.060	2.967	2.880	2.798	2.720	2.646	2.577	2.511	2.448	2.388	2.331	2.277	2.225	2.176	2.128	2.083	2.040	1.998	1.958
101	3.293	3.187	3.087	2.994	2.906	2.823	2.744	2.670	2.600	2.533	2.470	2.410	2.352	2.298	2.245	2.196	2.148	2.102	2.058	2.016	1.976
102	3.323	3.215	3.115	3.021	2.932	2.848	2.769	2.694	2.623	2.556	2.492	2.431	2.373	2.318	2.265	2.215	2.167	2.121	2.077	2.034	1.994
103	3.352	3.244	3.142	3.047	2.957	2.873	2.793	2.718	2.646	2.578	2.514	2.453	2.394	2.338	2.285	2.235	2.186	2.139	2.095	2.052	2.011
104	3.381	3.272	3.170	3.074	2.983	2.898	2.817	2.741	2.669	2.601	2.536	2.474	2.415	2.359	2.305	2.254	2.205	2.158	2.113	2.070	2.029
105	3.410	3.300	3.197	3.100	3.009	2.923	2.842	2.765	2.692	2.623	2.558	2.495	2.436	2.379	2.325	2.273	2.224	2.177	2.131	2.088	2.046
106	3.439	3.328	3.224	3.126	3.034	2.948	2.866	2.788	2.715	2.645	2.579	2.516	2.456	2.399	2.345	2.293	2.243	2.195	2.149	2.106	2.063
107	3.468	3.356	3.251	3.153	3.060	2.973	2.890	2.812	2.738	2.668	2.601	2.538	2.477	2.419	2.365	2.312	2.262	2.214	2.167	2.123	2.081
108	3.497	3.384	3.278	3.179	3.085	2.997	2.914	2.835	2.761	2.690	2.623	2.559	2.498	2.440	2.384	2.331	2.281	2.232	2.186	2.141	2.098
109	3.526	3.412	3.305	3.205	3.111	3.022	2.938	2.859	2.783	2.712	2.644	2.580	2.518	2.460	2.404	2.350	2.299	2.250	2.204	2.159	2.115
110	3.554	3.440	3.332	3.231	3.136	3.047	2.962	2.882	2.806	2.734	2.666	2.601	2.539	2.480	2.423	2.370	2.318	2.269	2.222	2.176	2.133
111	3.583	3.468	3.359	3.257	3.162	3.071	2.986	2.905	2.829	2.756	2.687	2.622	2.559	2.500	2.443	2.389	2.337	2.287	2.239	2.194	2.150
112	3.612	3.495	3.386	3.283	3.187	3.096	3.010	2.928	2.851	2.778	2.709	2.643	2.580	2.520	2.463	2.408	2.356	2.305	2.257	2.211	2.167
113	3.640	3.523	3.413	3.309	3.212	3.120	3.034	2.952	2.874	2.800	2.730	2.664	2.600	2.540	2.482	2.427	2.374	2.324	2.275	2.229	2.184
114	3.669	3.551	3.440	3.335	3.237	3.145	3.057	2.975	2.897	2.822	2.752	2.685	2.621	2.560	2.502	2.446	2.393	2.342	2.293	2.246	2.201
115	3.698	3.579	3.466	3.361	3.263	3.169	3.081	2.998	2.919	2.844	2.773	2.705	2.641	2.580	2.521	2.465	2.411	2.360	2.311	2.264	2.219
116	3.726	3.606	3.493	3.387	3.288	3.194	3.105	3.021	2.942	2.866	2.794	2.726	2.661	2.600	2.540	2.484	2.430	2.378	2.329	2.281	2.236
117	3.754	3.633	3.520	3.413	3.313	3.218	3.129	3.044	2.964	2.888	2.816	2.747	2.682	2.619	2.560	2.503	2.449	2.396	2.347	2.299	2.253
118	3.783	3.661	3.546	3.439	3.338	3.242	3.152	3.067	2.986	2.910	2.837	2.768	2.702	2.639	2.579	2.522	2.467	2.415	2.364	2.316	2.270
119	3.811	3.688	3.573	3.465	3.363	3.267	3.176	3.090	3.009	2.932	2.858	2.789	2.722	2.659	2.599	2.541	2.486	2.433	2.382	2.333	2.287
120	3.840	3.716	3.600	3.491	3.388	3.291	3.200	3.113	3.031	2.954	2.880	2.809	2.743	2.679	2.618	2.560	2.504	2.451	2.400	2.351	2.304

Fig. 10f

mCi per cGy matrix

Total Bod
Lean Bod
|
V

T-1/2[hr]-effective -> A0 [mCi/cGy]

mass[Kg]	51	52	53	54	55	56	57	58	59	60	61	62	63	64	65	66	67	68	69	70	71
84	1.641	1.610	1.579	1.550	1.522	1.495	1.468	1.443	1.419	1.395	1.372	1.350	1.329	1.308	1.288	1.268	1.249	1.231	1.213	1.196	1.179
85	1.659	1.627	1.596	1.566	1.538	1.511	1.484	1.458	1.434	1.410	1.387	1.364	1.343	1.322	1.301	1.282	1.263	1.244	1.226	1.208	1.191
86	1.676	1.644	1.613	1.583	1.554	1.526	1.500	1.474	1.449	1.425	1.401	1.379	1.357	1.336	1.315	1.295	1.276	1.257	1.239	1.221	1.204
87	1.693	1.661	1.629	1.599	1.570	1.542	1.515	1.489	1.464	1.439	1.416	1.393	1.371	1.349	1.329	1.308	1.289	1.270	1.252	1.234	1.216
88	1.711	1.678	1.646	1.616	1.586	1.558	1.531	1.504	1.479	1.454	1.430	1.407	1.385	1.363	1.342	1.322	1.302	1.283	1.265	1.246	1.229
89	1.728	1.695	1.663	1.632	1.603	1.574	1.546	1.520	1.494	1.469	1.445	1.422	1.399	1.377	1.356	1.335	1.316	1.296	1.277	1.259	1.241
90	1.746	1.712	1.680	1.649	1.619	1.590	1.562	1.535	1.509	1.484	1.460	1.436	1.413	1.391	1.370	1.349	1.329	1.309	1.290	1.272	1.254
91	1.763	1.729	1.697	1.665	1.635	1.606	1.578	1.550	1.524	1.499	1.474	1.450	1.427	1.405	1.383	1.362	1.342	1.322	1.303	1.285	1.266
92	1.781	1.746	1.713	1.682	1.651	1.622	1.593	1.566	1.539	1.513	1.489	1.465	1.441	1.419	1.397	1.376	1.355	1.335	1.316	1.297	1.279
93	1.798	1.763	1.730	1.698	1.667	1.638	1.609	1.581	1.554	1.528	1.503	1.479	1.456	1.433	1.411	1.389	1.369	1.349	1.329	1.310	1.292
94	1.815	1.781	1.747	1.715	1.683	1.653	1.624	1.596	1.569	1.543	1.518	1.493	1.470	1.447	1.424	1.403	1.382	1.362	1.342	1.323	1.304
95	1.833	1.798	1.764	1.731	1.700	1.669	1.640	1.612	1.584	1.558	1.532	1.508	1.484	1.461	1.438	1.416	1.395	1.375	1.355	1.335	1.317
96	1.850	1.815	1.781	1.748	1.716	1.685	1.656	1.627	1.599	1.573	1.547	1.522	1.498	1.475	1.452	1.430	1.409	1.388	1.368	1.348	1.329
97	1.868	1.832	1.797	1.764	1.732	1.701	1.671	1.642	1.615	1.588	1.562	1.536	1.512	1.488	1.466	1.443	1.422	1.401	1.381	1.361	1.342
98	1.885	1.849	1.814	1.780	1.748	1.717	1.687	1.658	1.630	1.602	1.576	1.551	1.526	1.502	1.479	1.457	1.435	1.414	1.393	1.374	1.354
99	1.903	1.866	1.831	1.797	1.764	1.733	1.702	1.673	1.645	1.617	1.591	1.565	1.540	1.516	1.493	1.470	1.448	1.427	1.406	1.386	1.367
100	1.920	1.883	1.847	1.813	1.780	1.748	1.718	1.688	1.660	1.632	1.605	1.579	1.554	1.530	1.506	1.484	1.461	1.440	1.419	1.399	1.379
101	1.937	1.900	1.864	1.830	1.796	1.764	1.733	1.703	1.675	1.647	1.620	1.594	1.568	1.544	1.520	1.497	1.475	1.453	1.432	1.411	1.392
102	1.954	1.917	1.881	1.846	1.812	1.780	1.749	1.719	1.689	1.661	1.634	1.608	1.582	1.557	1.533	1.510	1.488	1.466	1.445	1.424	1.404
103	1.972	1.934	1.897	1.862	1.828	1.796	1.764	1.734	1.704	1.676	1.649	1.622	1.596	1.571	1.547	1.524	1.501	1.479	1.457	1.436	1.416
104	1.989	1.951	1.914	1.878	1.844	1.811	1.780	1.749	1.719	1.690	1.663	1.636	1.610	1.585	1.560	1.537	1.514	1.492	1.470	1.449	1.429
105	2.006	1.967	1.930	1.894	1.860	1.827	1.795	1.764	1.734	1.705	1.677	1.650	1.624	1.598	1.574	1.550	1.527	1.504	1.483	1.461	1.441
106	2.023	1.984	1.947	1.911	1.876	1.842	1.810	1.779	1.749	1.720	1.691	1.664	1.638	1.612	1.587	1.563	1.540	1.517	1.495	1.474	1.453
107	2.040	2.001	1.963	1.927	1.892	1.858	1.825	1.794	1.763	1.734	1.706	1.678	1.651	1.626	1.601	1.576	1.553	1.530	1.508	1.486	1.465
108	2.057	2.017	1.979	1.943	1.907	1.873	1.840	1.809	1.778	1.748	1.720	1.692	1.665	1.639	1.614	1.589	1.566	1.543	1.520	1.499	1.478
109	2.074	2.034	1.996	1.959	1.923	1.889	1.856	1.824	1.793	1.763	1.734	1.706	1.679	1.653	1.627	1.603	1.579	1.555	1.533	1.511	1.490
110	2.091	2.051	2.012	1.975	1.939	1.904	1.871	1.838	1.807	1.777	1.748	1.720	1.693	1.666	1.640	1.616	1.592	1.568	1.545	1.523	1.502
111	2.108	2.067	2.028	1.991	1.954	1.920	1.886	1.853	1.822	1.792	1.762	1.734	1.706	1.680	1.654	1.629	1.604	1.581	1.558	1.536	1.514
112	2.125	2.084	2.044	2.007	1.970	1.935	1.901	1.868	1.837	1.806	1.776	1.748	1.720	1.693	1.667	1.642	1.617	1.593	1.570	1.548	1.526
113	2.141	2.100	2.061	2.022	1.986	1.950	1.916	1.883	1.851	1.820	1.790	1.761	1.734	1.706	1.680	1.655	1.630	1.606	1.583	1.560	1.538
114	2.158	2.117	2.077	2.038	2.001	1.965	1.931	1.898	1.866	1.834	1.804	1.775	1.747	1.720	1.693	1.668	1.643	1.619	1.595	1.572	1.550
115	2.175	2.133	2.093	2.054	2.017	1.981	1.946	1.913	1.880	1.849	1.819	1.789	1.761	1.733	1.707	1.681	1.656	1.631	1.608	1.585	1.562
116	2.192	2.150	2.109	2.070	2.032	1.996	1.961	1.927	1.895	1.863	1.832	1.803	1.774	1.747	1.720	1.694	1.668	1.644	1.620	1.597	1.574
117	2.209	2.166	2.125	2.086	2.048	2.011	1.976	1.942	1.909	1.877	1.846	1.817	1.788	1.760	1.733	1.707	1.681	1.656	1.632	1.609	1.586
118	2.225	2.182	2.141	2.102	2.063	2.027	1.991	1.957	1.923	1.891	1.860	1.830	1.801	1.773	1.746	1.719	1.694	1.669	1.645	1.621	1.598
119	2.242	2.199	2.157	2.117	2.079	2.042	2.006	1.971	1.938	1.906	1.874	1.844	1.815	1.787	1.759	1.732	1.707	1.681	1.657	1.633	1.610
120	2.259	2.215	2.173	2.133	2.094	2.057	2.021	1.986	1.952	1.920	1.888	1.858	1.828	1.800	1.772	1.745	1.719	1.694	1.669	1.646	1.622

Fig. 10g

mCi per cGy matrix

Total Bod
Lean Bod
|
V

T-1/2[hr]-effective --> A0 [mCi/cGy]

mass[Kg]	72	73	74	75	76	77	78	79	80	81	82	83	84	85	86	87	88	89	90	91	92
84	1.163	1.147	1.131	1.116	1.101	1.087	1.073	1.060	1.046	1.033	1.021	1.008	0.996	0.985	0.973	0.962	0.951	0.940	0.930	0.920	0.910
85	1.175	1.159	1.143	1.128	1.113	1.099	1.084	1.071	1.057	1.044	1.032	1.019	1.007	0.995	0.984	0.972	0.961	0.950	0.940	0.930	0.919
86	1.187	1.171	1.155	1.140	1.125	1.110	1.096	1.082	1.068	1.055	1.042	1.030	1.018	1.006	0.994	0.983	0.971	0.960	0.950	0.939	0.929
87	1.200	1.183	1.167	1.152	1.136	1.122	1.107	1.093	1.080	1.066	1.053	1.041	1.029	1.016	1.004	0.993	0.981	0.970	0.960	0.949	0.939
88	1.212	1.195.	1.179	1.163	1.148	1.133	1.119	1.104	1.091	1.077	1.064	1.051	1.039	1.027	1.015	1.003	0.992	0.980	0.969	0.959	0.948
89	1.224	1.207	1.191	1.175	1.160	1.145	1.130	1.116	1.102	1.088	1.075	1.062	1.049	1.037	1.025	1.013	1.002	0.990	0.979	0.969	0.958
90	1.237	1.220	1.203	1.187	1.171	1.156	1.141	1.127	1.113	1.099	1.086	1.073	1.060	1.047	1.035	1.023	1.012	1.000	0.989	0.978	0.968
91	1.249	1.232	1.215	1.199	1.183	1.168	1.153	1.138	1.124	1.110	1.097	1.083	1.070	1.058	1.046	1.034	1.022	1.010	0.999	0.988	0.977
92	1.261	1.244	1.227	1.211	1.195	1.179	1.164	1.149	1.135	1.121	1.107	1.094	1.081	1.069	1.056	1.044	1.032	1.020	1.009	0.998	0.987
93	1.274	1.256	1.239	1.223	1.207	1.191	1.176	1.161	1.146	1.132	1.118	1.105	1.092	1.079	1.066	1.054	1.042	1.030	1.019	1.008	0.997
94	1.286	1.268	1.251	1.235	1.219	1.202	1.187	1.172	1.157	1.143	1.129	1.116	1.102	1.089	1.077	1.064	1.052	1.040	1.029	1.017	1.006
95	1.298	1.281	1.263	1.246	1.230	1.214	1.198	1.183	1.168	1.154	1.140	1.126	1.113	1.100	1.087	1.074	1.062	1.050	1.039	1.027	1.016
96	1.311	1.293	1.275	1.258	1.242	1.226	1.210	1.195	1.180	1.165	1.151	1.137	1.123	1.110	1.097	1.085	1.072	1.060	1.049	1.037	1.026
97	1.323	1.305	1.287	1.270	1.253	1.237	1.221	1.206	1.191	1.176	1.162	1.148	1.134	1.121	1.108	1.095	1.082	1.070	1.059	1.047	1.035
98	1.335	1.317	1.299	1.282	1.265	1.249	1.233	1.217	1.202	1.187	1.173	1.159	1.145	1.131	1.118	1.105	1.093	1.080	1.068	1.057	1.045
99	1.348	1.329	1.311	1.294	1.277	1.260	1.244	1.228	1.213	1.198	1.183	1.169	1.155	1.142	1.129	1.116	1.103	1.090	1.078	1.066	1.055
100	1.360	1.341	1.323	1.306	1.288	1.272	1.255	1.239	1.224	1.209	1.194	1.180	1.166	1.152	1.139	1.125	1.113	1.100	1.088	1.076	1.064
101	1.372	1.353	1.335	1.317	1.300	1.283	1.267	1.251	1.235	1.220	1.205	1.190	1.176	1.162	1.149	1.136	1.123	1.110	1.098	1.086	1.074
102	1.384	1.365	1.347	1.329	1.312	1.295	1.279	1.262	1.246	1.231	1.216	1.201	1.187	1.173	1.159	1.146	1.133	1.120	1.108	1.095	1.083
103	1.397	1.377	1.359	1.341	1.323	1.306	1.290	1.273	1.257	1.241	1.226	1.211	1.197	1.183	1.169	1.156	1.143	1.130	1.117	1.105	1.093
104	1.409	1.389	1.371	1.352	1.335	1.317	1.300	1.284	1.268	1.252	1.237	1.222	1.207	1.193	1.179	1.166	1.153	1.140	1.127	1.115	1.102
105	1.421	1.401	1.382	1.364	1.346	1.329	1.312	1.295	1.279	1.263	1.248	1.233	1.218	1.204	1.190	1.176	1.163	1.149	1.137	1.124	1.112
106	1.433	1.413	1.394	1.376	1.358	1.340	1.323	1.306	1.290	1.274	1.258	1.243	1.228	1.214	1.200	1.186	1.172	1.159	1.146	1.134	1.121
107	1.445	1.425	1.406	1.387	1.369	1.351	1.334	1.317	1.300	1.284	1.269	1.253	1.238	1.224	1.210	1.196	1.182	1.169	1.156	1.143	1.131
108	1.457	1.437	1.418	1.399	1.380	1.362	1.345	1.328	1.311	1.295	1.279	1.264	1.248	1.234	1.220	1.206	1.192	1.179	1.166	1.153	1.140
109	1.469	1.449	1.429	1.410	1.392	1.374	1.356	1.339	1.322	1.306	1.290	1.274	1.259	1.244	1.230	1.216	1.202	1.188	1.175	1.162	1.150
110	1.481	1.461	1.441	1.422	1.403	1.385	1.367	1.350	1.333	1.316	1.300	1.285	1.269	1.254	1.240	1.226	1.212	1.198	1.185	1.172	1.159
111	1.493	1.473	1.453	1.433	1.414	1.396	1.379	1.361	1.344	1.327	1.311	1.295	1.280	1.265	1.250	1.236	1.222	1.208	1.194	1.181	1.169
112	1.505	1.484	1.464	1.445	1.426	1.407	1.389	1.372	1.354	1.338	1.321	1.305	1.290	1.275	1.260	1.245	1.231	1.217	1.204	1.191	1.178
113	1.517	1.496	1.476	1.456	1.437	1.419	1.400	1.382	1.365	1.348	1.332	1.316	1.300	1.285	1.270	1.255	1.241	1.227	1.213	1.200	1.187
114	1.529	1.508	1.487	1.468	1.448	1.429	1.411	1.393	1.376	1.359	1.342	1.326	1.310	1.295	1.280	1.265	1.251	1.237	1.223	1.210	1.196
115	1.541	1.520	1.499	1.479	1.460	1.441	1.422	1.404	1.387	1.369	1.353	1.336	1.321	1.305	1.290	1.275	1.261	1.246	1.233	1.219	1.206
116	1.552	1.531	1.511	1.490	1.471	1.452	1.433	1.415	1.397	1.380	1.363	1.347	1.331	1.315	1.300	1.285	1.270	1.256	1.242	1.228	1.215
117	1.564	1.543	1.522	1.502	1.482	1.463	1.444	1.426	1.408	1.391	1.374	1.357	1.341	1.325	1.310	1.295	1.280	1.266	1.251	1.238	1.224
118	1.576	1.555	1.534	1.513	1.493	1.474	1.455	1.437	1.418	1.401	1.384	1.367	1.351	1.335	1.320	1.304	1.290	1.275	1.261	1.247	1.234
119	1.588	1.566	1.545	1.525	1.504	1.485	1.466	1.447	1.429	1.412	1.394	1.378	1.361	1.345	1.330	1.314	1.299	1.285	1.270	1.256	1.243
120	1.600	1.578	1.557	1.536	1.516	1.496	1.477	1.458	1.440	1.422	1.405	1.388	1.371	1.355	1.339	1.324	1.309	1.294	1.280	1.266	1.252

Fig. 10h

mCi per cGy matrix

Total Bod
Lean Bod
|
V

mass[Kg]	T-1/2[hr]-effective --> 93	94	95	96	97	98	A0 [mCi/cGy] 99	100
84	0.900	0.890	0.881	0.872	0.863	0.854	0.845	0.837
85	0.910	0.900	0.890	0.881	0.872	0.863	0.854	0.846
86	0.919	0.909	0.900	0.890	0.881	0.872	0.863	0.855
87	0.929	0.919	0.909	0.900	0.890	0.881	0.872	0.864
88	0.938	0.928	0.918	0.909	0.900	0.890	0.881	0.873
89	0.948	0.938	0.928	0.918	0.909	0.899	0.890	0.881
90	0.957	0.947	0.937	0.927	0.918	0.908	0.899	0.890
91	0.967	0.957	0.947	0.937	0.927	0.918	0.909	0.898
92	0.976	0.966	0.956	0.946	0.936	0.927	0.917	0.908
93	0.986	0.976	0.965	0.955	0.946	0.936	0.926	0.917
94	0.996	0.985	0.975	0.964	0.955	0.945	0.935	0.926
95	1.005	0.994	0.984	0.974	0.964	0.954	0.944	0.935
96	1.015	1.004	0.993	0.983	0.973	0.963	0.953	0.944
97	1.024	1.013	1.003	0.992	0.982	0.972	0.962	0.953
98	1.034	1.023	1.012	1.002	0.991	0.981	0.971	0.961
99	1.043	1.032	1.021	1.011	1.000	0.990	0.980	0.970
100	1.053	1.042	1.031	1.020	1.009	0.999	0.989	0.979
101	1.062	1.051	1.040	1.029	1.018	1.008	0.998	0.988
102	1.072	1.060	1.049	1.039	1.028	1.017	1.007	0.997
103	1.081	1.070	1.059	1.047	1.037	1.026	1.016	1.006
104	1.091	1.079	1.068	1.057	1.046	1.035	1.025	1.014
105	1.100	1.089	1.077	1.066	1.055	1.044	1.033	1.023
106	1.109	1.098	1.086	1.075	1.064	1.053	1.042	1.032
107	1.119	1.107	1.095	1.084	1.073	1.062	1.051	1.040
108	1.128	1.116	1.104	1.093	1.081	1.070	1.060	1.049
109	1.137	1.125	1.113	1.102	1.090	1.079	1.068	1.058
110	1.147	1.134	1.122	1.111	1.099	1.088	1.077	1.066
111	1.156	1.144	1.132	1.120	1.108	1.097	1.086	1.075
112	1.165	1.153	1.141	1.129	1.117	1.106	1.094	1.084
113	1.174	1.162	1.150	1.138	1.126	1.114	1.103	1.092
114	1.184	1.171	1.159	1.147	1.135	1.123	1.112	1.101
115	1.193	1.180	1.168	1.155	1.144	1.132	1.120	1.109
116	1.202	1.189	1.177	1.164	1.152	1.141	1.129	1.118
117	1.211	1.198	1.186	1.173	1.161	1.149	1.138	1.126
118	1.220	1.207	1.195	1.182	1.170	1.158	1.146	1.135
119	1.229	1.216	1.204	1.191	1.179	1.167	1.155	1.143
120	1.239	1.225	1.213	1.200	1.188	1.175	1.164	1.152

3-D mCi per cGy

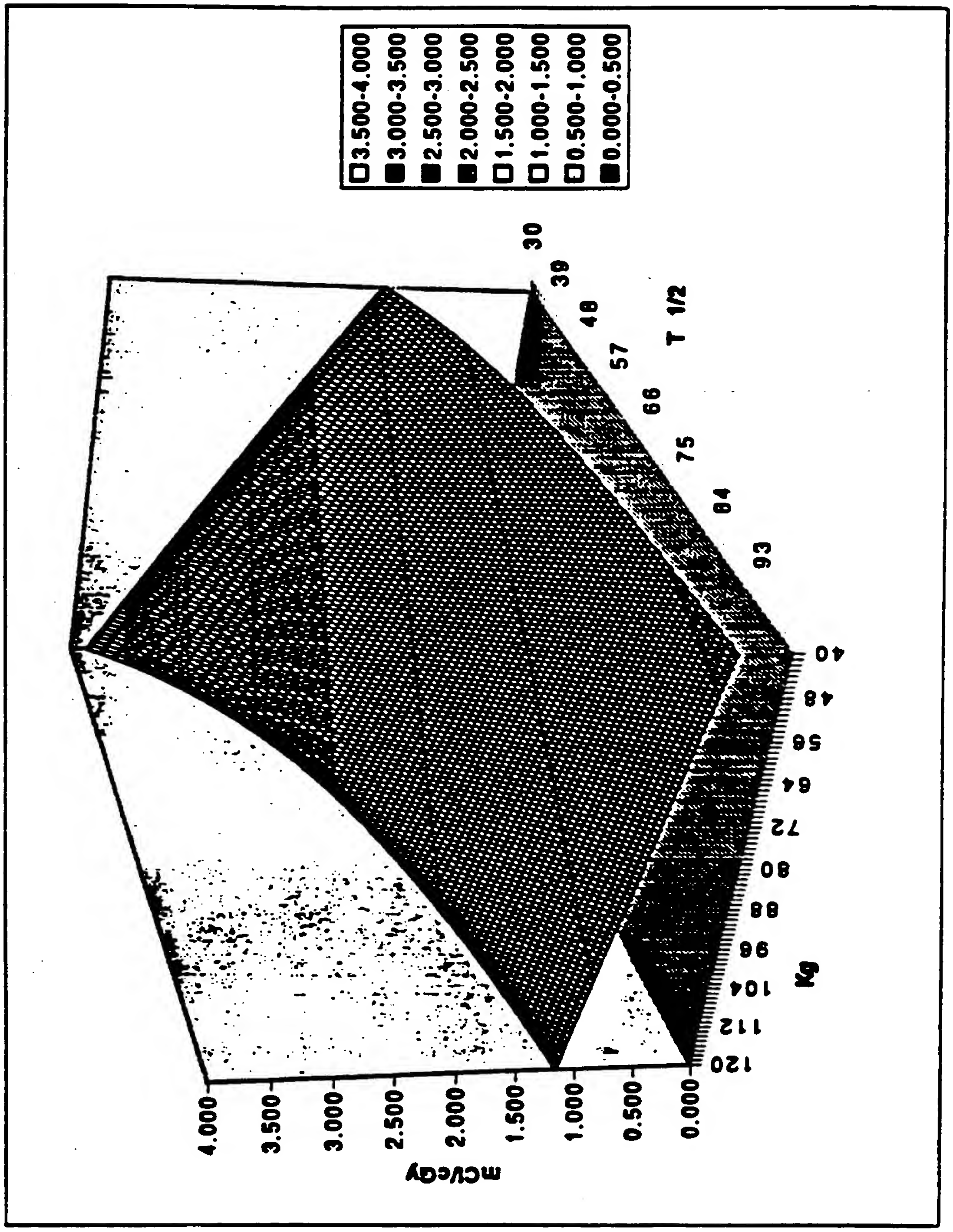


Fig. 11

toxicity_noBMT.txt

pt num	mCi	TB-kg	TB-dose	Blood-dose	marrow-dos	LBM	tox-grade	mCiperKG	mCipermsq	mCiperLBM	TBLBMdose
1	66.0	72.8	25.0	126	51	74.606	1	0.907	34.8	0.885	25.8
2	45.1	77.2	25.0	141	55	69.2	0	0.584	23.7	0.652	28.2
4	57.0	80.8	25.0	166	64	66.974	1	0.705	29.6	0.851	31.4
5	38.0	74.9	35.0	186	76	74.924	1	0.507	19.8	0.507	33.6
6	40.0	81.3	35.0	257	99	81.39	1	0.492	19.6	0.491	34.6
7	41.0	82.6	35.0	126	60	81.602	0	0.496	20.0	0.502	37.6
8	39.8	84.2	35.0	146	67	71.002	2	0.473	20.0	0.561	42.4
9	43.5	66.0	45.0	269	104	54.042	0	0.659	26.0	0.805	55.9
10	61.5	90.0	45.0	291	118	77.68	0	0.683	29.3	0.792	52.2
13	40.5	60.5	45.0	293	112	55.965	0	0.669	24.5	0.724	50.7
14	68.3	83.3	55.0	305	127	73.334	0	0.820	34.2	0.931	64.3
15	44.1	54.4	55.0	265	105	58.24	3	0.811	27.6	0.757	53.7
16	70.9	93.4	55.0	381	153	73.97	2	0.759	33.7	0.958	70.1
19	68.5	82.3	65.0	370	158	56.602	1	0.832	36.2	1.210	92.2
24	106.7	83.1	75.0	340	148	83.934	0	1.284	51.4	1.271	71.4
27	97.9	73.0	85.0	443	187	57.785	0	1.341	54.2	1.694	108.5
28	95.6	86.4	85.0	228	121	79.164	4	1.106	46.1	1.208	97.5
29	161.0	136.0	85.0	474	241	70.343	4	1.184	64.5	2.289	164.4
31	107.5	91.8	75.0	232	120	70.578	3	1.171	52.2	1.523	108.4
32	56.8	48.0	75.0	457	169	47.32	0	1.183	39.6	1.200	80.0
34	102.5	88.6	75.0	517	205	78.74	2	1.157	49.0	1.302	82.6

Fig. 12

Fig. 13

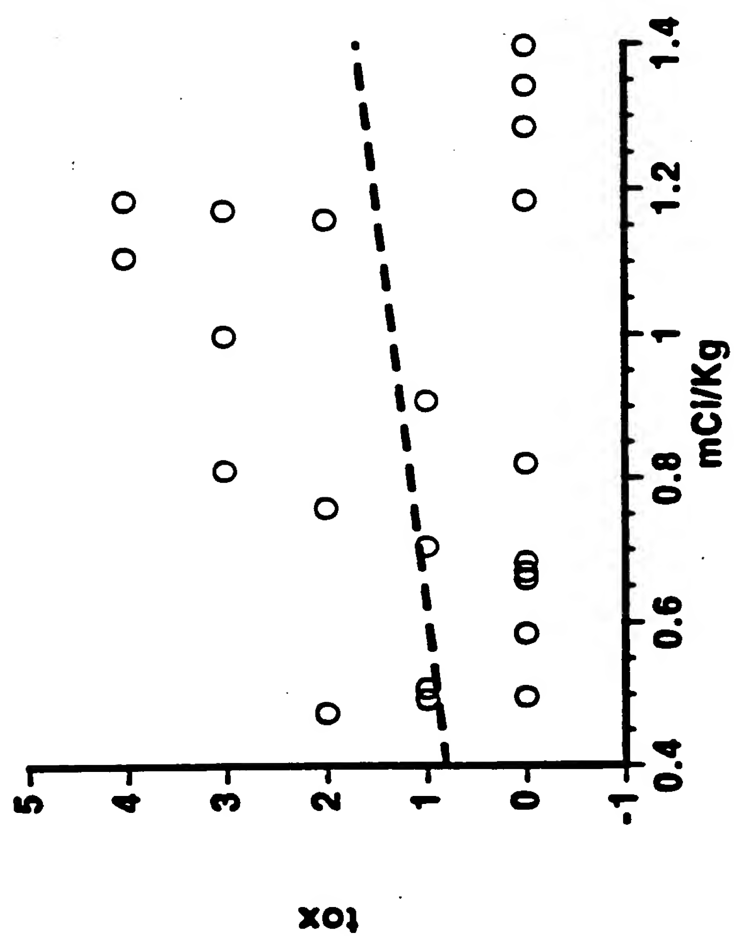


Fig. 14

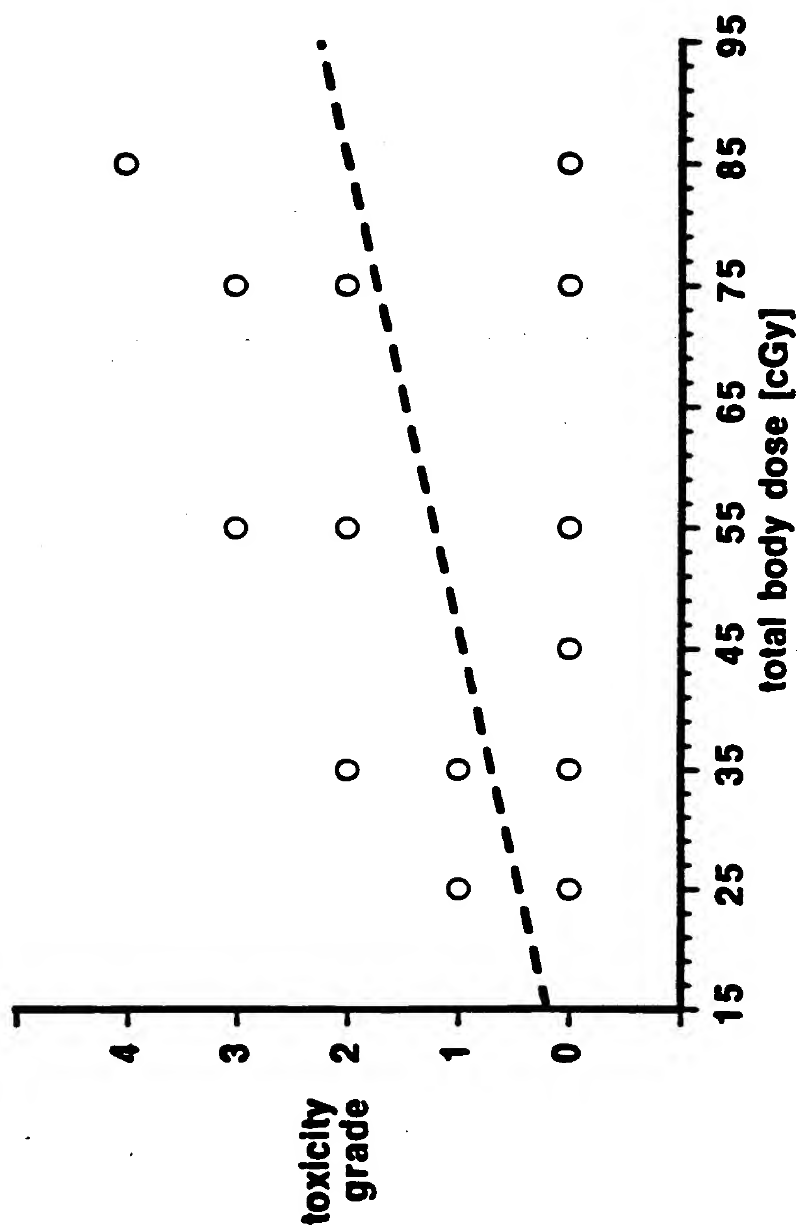
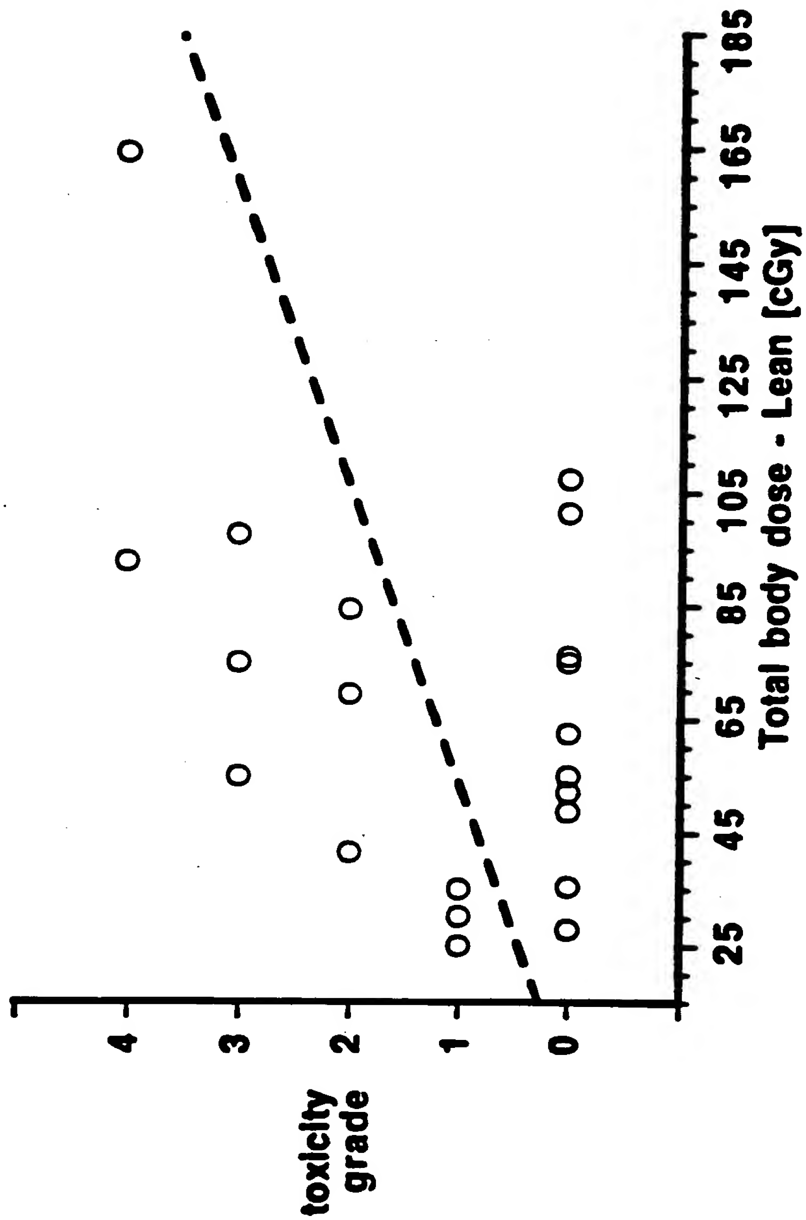

toxicity grade
0
1
2
3
4
15
25
35
45
55
65
75
85
95
total body dose [cGy]

Fig. 15


toxicity grade
0
1
2
3
4
25
45
65
85
105
125
145
165
185
Total body dose - Lean [cGy]

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US96/06240

A. CLASSIFICATION OF SUBJECT MATTER
IPC(6) :A61K 51/00; A61B 6/00; A61F 5/00
US CL :424/1.11, 1,65; 128/659; 604/20
According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED
Minimum documentation searched (classification system followed by classification symbols)
U.S. : 424/1.11, 1,65; 128/659; 604/20

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
APS, MEDLINE, BIOSIS, SCISEARCH, WPIDS

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	ZASADNY et al. Standardized Uptake Values of Normal Tissues at PET with 2-[Fluorine-18]-Fluoro-2-deoxy-D-glucose: Variations with Body Weight and a Method for Correction. Radiology. 01 December 1993, Vol. 189, No. 3, pages 847-850.	1-25
Y	KORAL et al. CT-SPECT Fusion Plus Conjugate Views for Determining Dosimetry in Iodine-131-Monoclonal Antibody Therapy of Lymphoma Patients. The Journal of Nuclear Medicine. Vol. 35, No. 10, 01 October 1994, pages 1714-1720.	1-25

[X] Further documents are listed in the continuation of Box C. [ ] See patent family annex.

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"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
18 JULY 1996	11 SEP 1996
Name and mailing address of the ISA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231	Authorized officer Michael G. Hartley
Facsimile No. (703) 305-3230	Telephone No. (703) 308-1235

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	KAMINSKY et al. Radioimmunotherapy of B-cell LYmphoma [I-131]Anti-B1 (Anti-CD20) Antibody. The New England Journal of Medicine, Vol. 329, No. 7, 12 August 1993, pages 459-465.	1-25